TRANSCODE

THERAPEUTICS™

The RNA Oncology Company

NASDAQ Symbol: RNAZ

Michael Dudley, CEO, Co-Founder

TRANSCODE

THERAPEUTICS™

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that clinical trials may be delayed; that the data reported may be interim data, conclusions as to which may be superseded by subsequent data we receive in connection with other and/or subsequent clinical trials; and that any anticipated meeting with or presentation to the FDA may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 Annual Report on Form 10-K 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.

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**

*Net Proceeds

NASDAQ Symbol: RNAZ	
Common Shares	12,977,234
Options (WAEP $0.77)	2,094,033
Underwriter Warrants (WAEP $5.00)	312,500
Total	**15,383,767**

Huge Unmet Need in Metastatic Cancer Treatment

Metastatic Cancer Reduces 5-year Survival
Critical Need for Therapy Targeting Metastasis*

90%

of Cancer Deaths Due to Metastasis

$111B

Global Metastatic Cancer Treatment Market by 2027

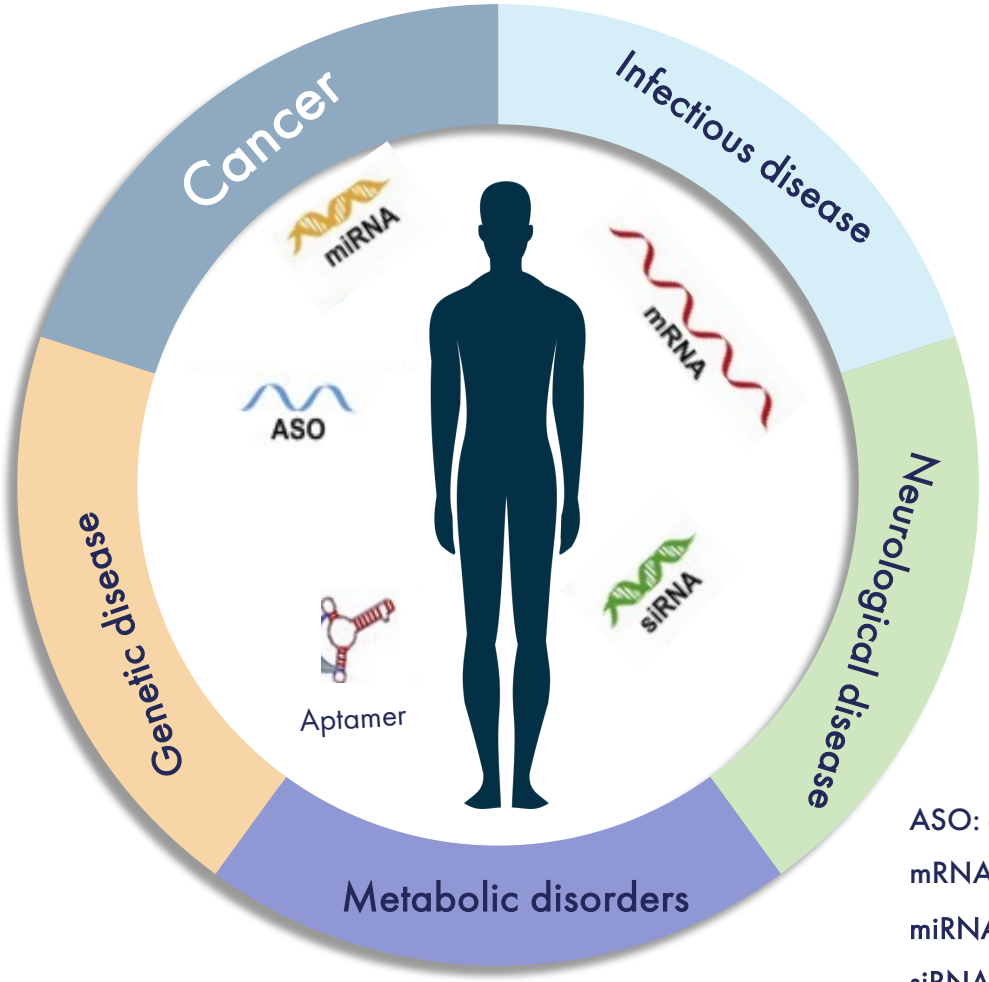
*Source: 2019 American Cancer Society, Inc., Surveillance Research

Power and Potential of RNA-based Therapies

RNA-based therapy holds the potential to target a vast number of genes and cellular pathways with high specificity*

Advantages of RNA treatments include:

- Access previously "undruggable" targets
- Rapid and cost-effective development
- Relatively easy to modify to address newly identified targets



ASO: antisense oligonucleotides
mRNA: messenger RNA
miRNA: microRNA
siRNA: short interfering RNA

*Liang X, et al. Biomed Pharmacother. 2020;125:109997.; Damase TR, et al. Frontiers in Bioengineering and Biotechnology. 2021;9.; Dowdy SF. Nat Biotechnol. 2017;35(3):222-229.

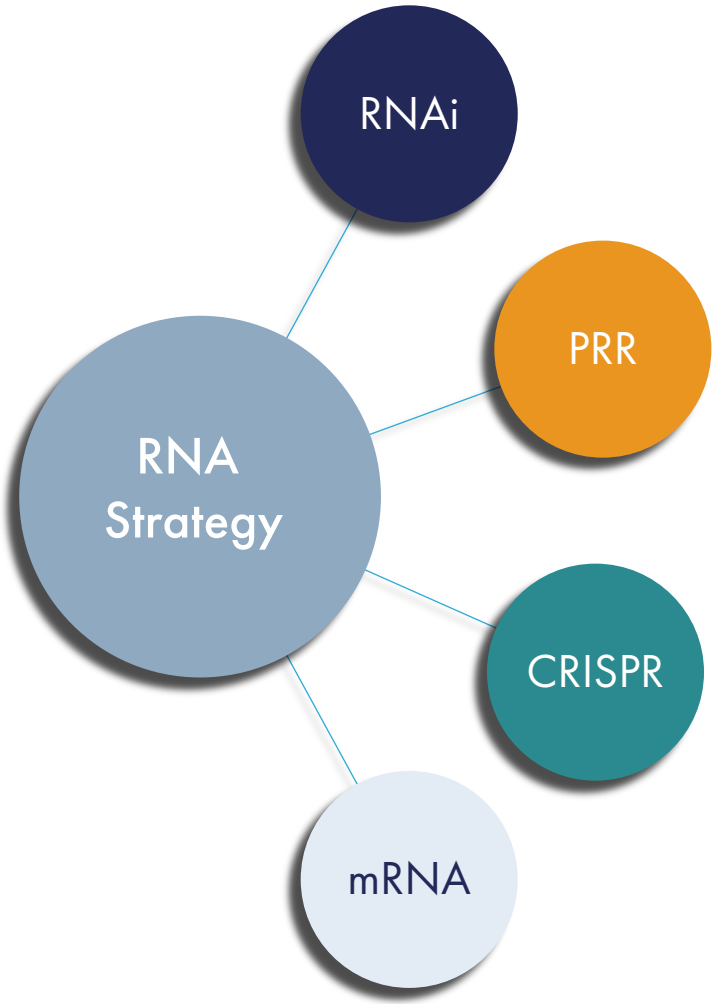
Challenge | # Oligonucleotide Therapeutics Efficiently Delivered to Genetic Targets

"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."

Robert S. Langer, ScD Institute Professor
David H. Koch Institute for Integrative Cancer Research
Massachusetts Institute of Technology

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

TransCode Therapeutics - The RNA Oncology Company



Defeating cancer requires many approaches

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

Resolving delivery challenge of RNA therapeutics

- Optimized delivery of RNA therapeutics to genetic targets in cancer
- 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

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

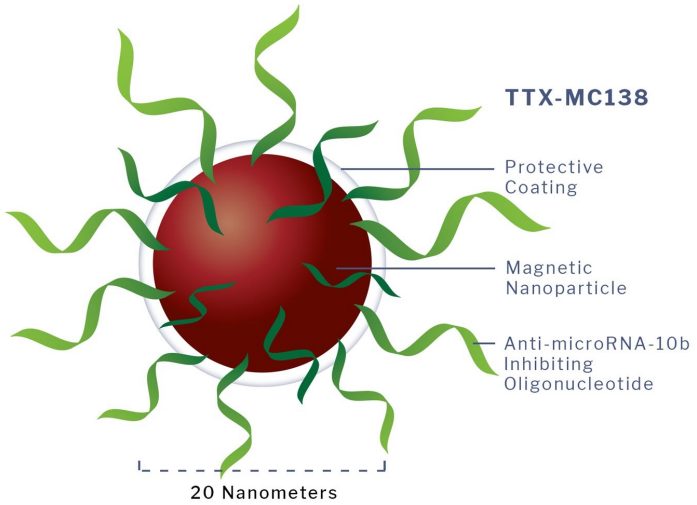
TransCode Therapeutics Approach

Develop RNA Therapeutics for Efficient Delivery to Genetic Targets in Cancer

Targeted RNA Therapeutics Using Proprietary Iron-Oxide Nanoparticle Delivery

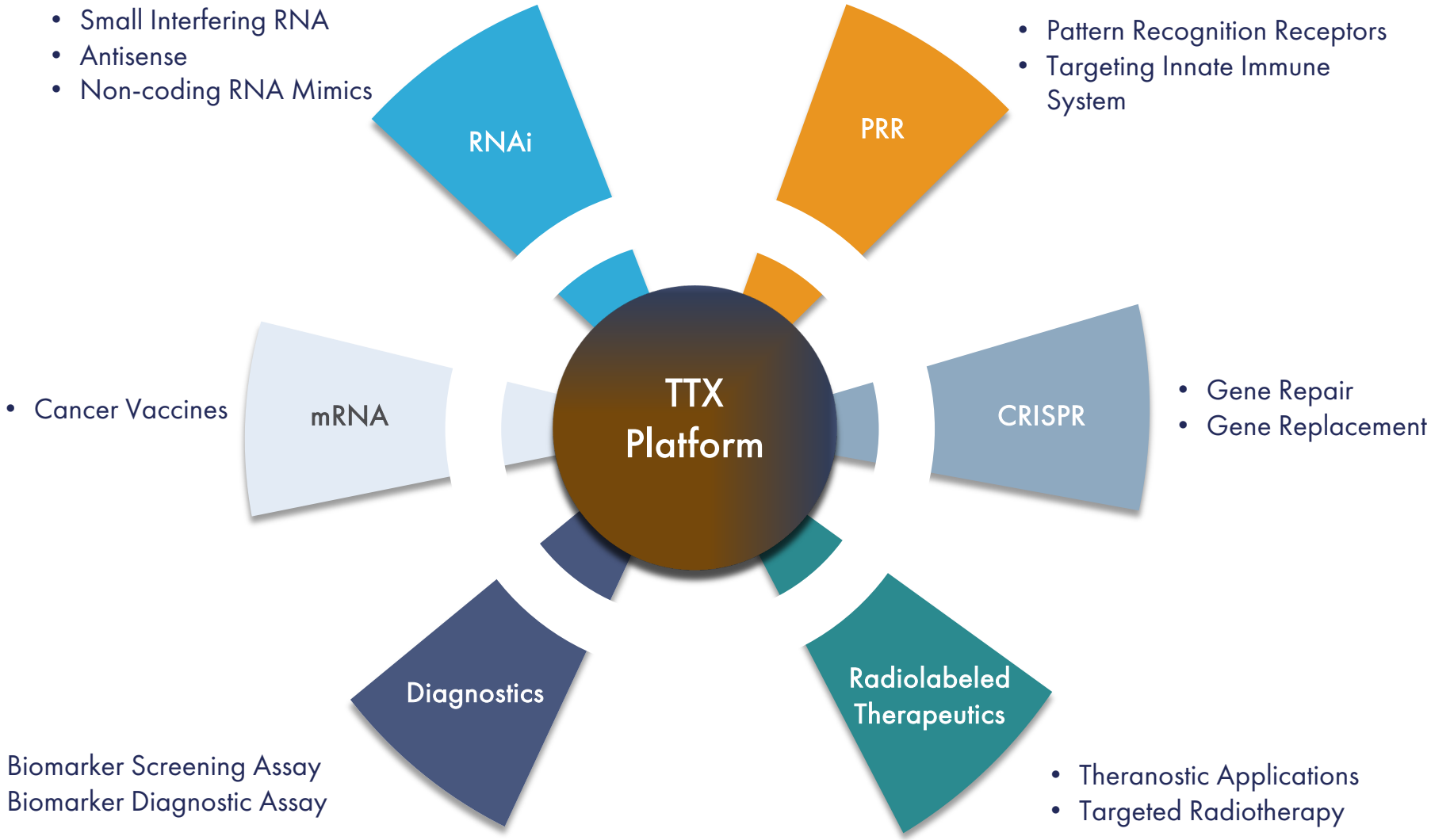
Our therapeutic strategy employs a nanoparticle extensively used in imaging that has been repurposed to:

- Deliver oligonucleotides to tumors and metastases
- Achieve robust target engagement inside tumor cells



We believe that demonstrating our ability to overcome the challenge of RNA therapeutic 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 and beyond

One Platform– Multiple RNA Approaches*



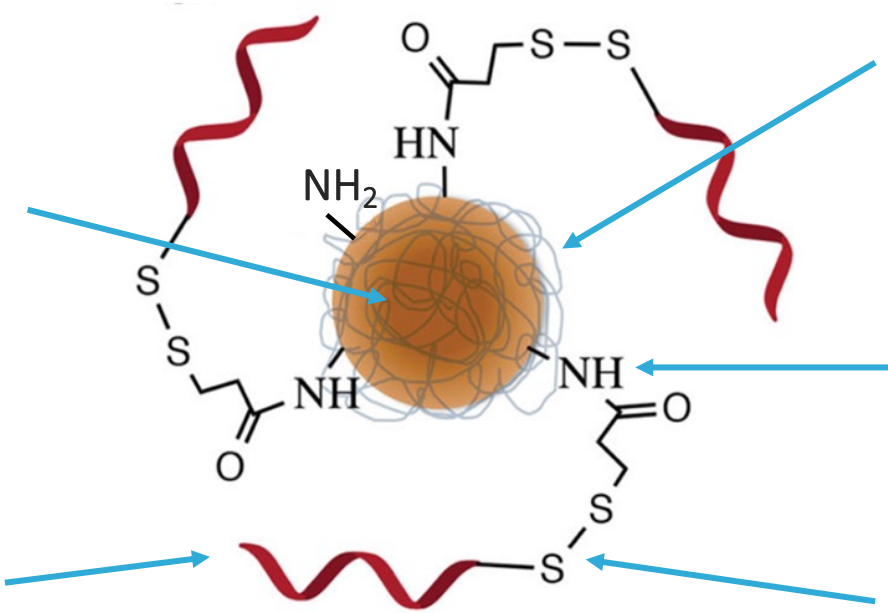
*In Oncology and beyond

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
- Unique capability to accumulate in tumor cells and metastatic sites
- Image capable via MRI
- Highly stable, low toxicity potential; low immunogenicity



Glucose Polymer (Dextran) coating:

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

Amino functional groups:

- Provide stabilization

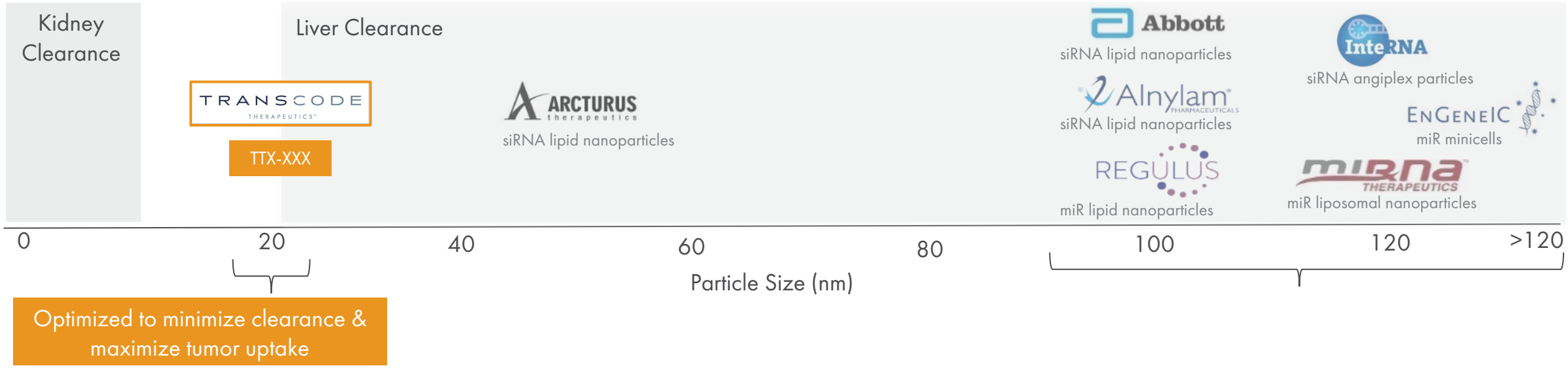
RNA-targeted nucleic acid:

- Strong binding affinity, specificity & stability while minimizing immunogenicity

Disulfide bond:

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

TTX Platform is Highly Differentiated



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 for Metastatic Disease

Validated Biomarker In A Metastatic Setting

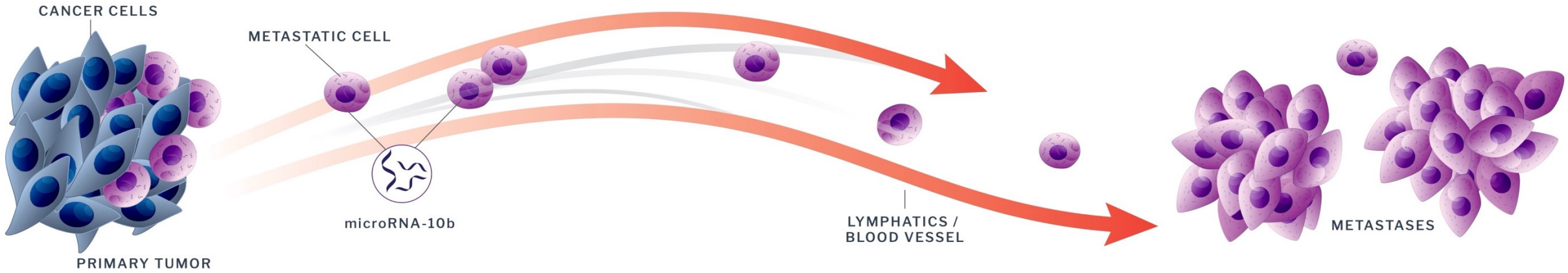
microRNA-10b (miR-10b) is a Unique, Well Documented Biomarker of Metastasis

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

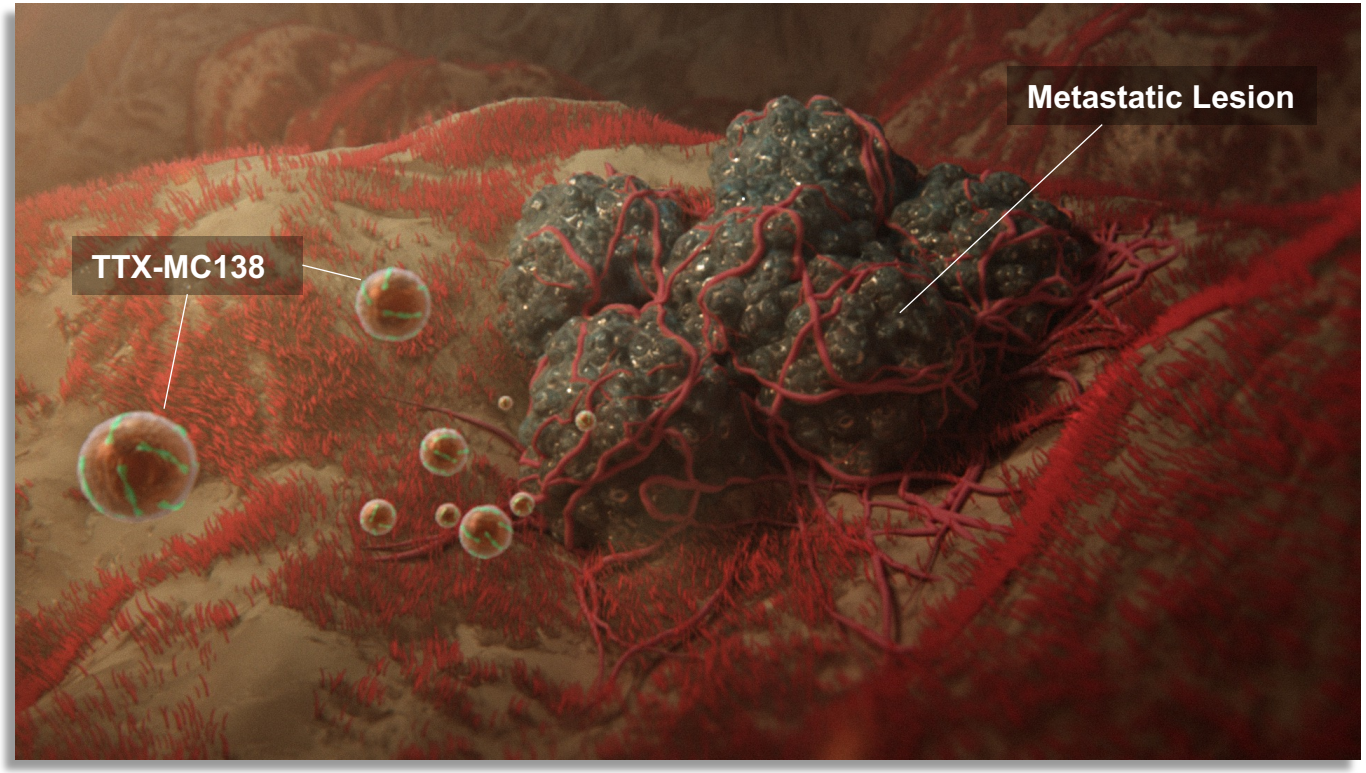
Biomarker of Metastasis

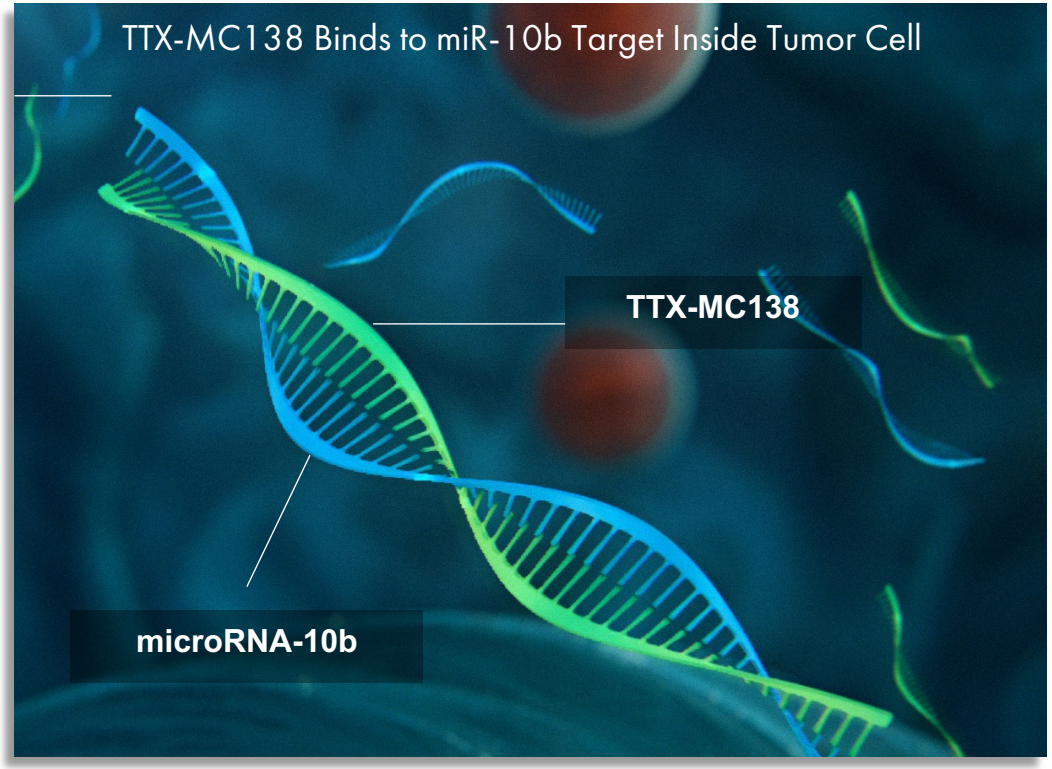
Linked to Higher Cancer Risk
Poor Survival Outcomes

Linked to Metastatic Progression in Multiple Cancer Types



TTX-MC138 - Designed to Inhibit miR-10b and Eliminate Metastasis





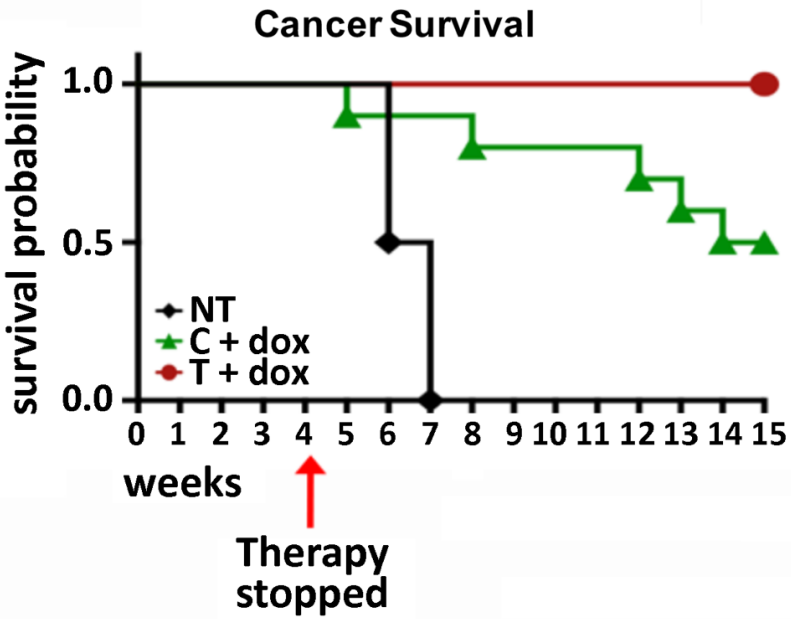
Cancer Res 75, 4407-4415 (2015); Sci Rep 7, 45060 (2017)

Survival Benefit Observed Preclinically in Multiple TNBC* Models

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

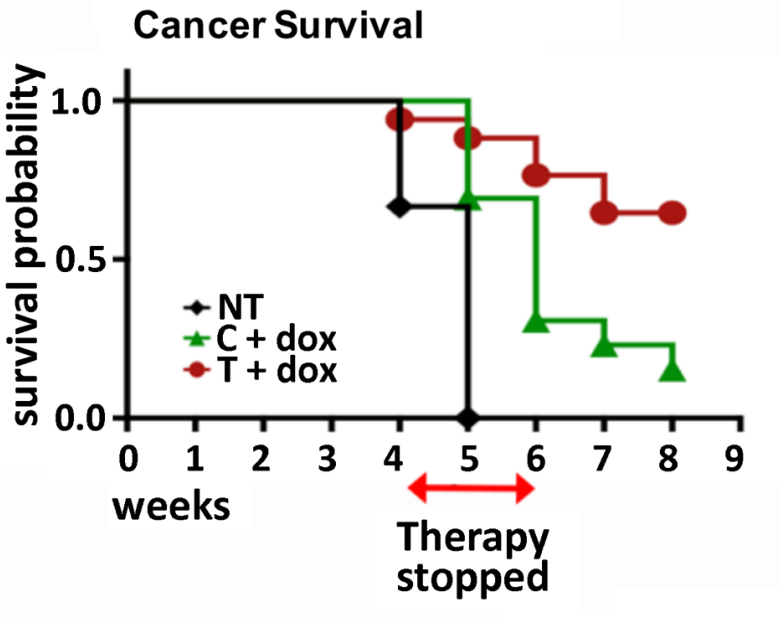


NT: No therapy, C: Control (Irrelevant oligo), T: TTX-MC138, dox: doxorubicin

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 TNBC: Triple Negative Breast Cancer

Path Forward

First In Human (FIH)
Phase 0 Study

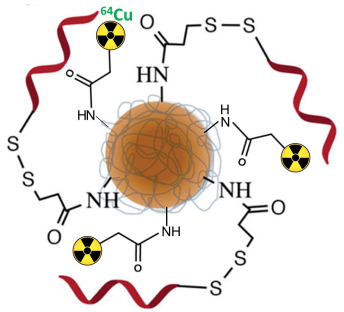
Microdosing Study in Breast Cancer Patients Using Radiolabeled TTX-MC138

Rethinking FIH trials :

*'Methods used to develop patient therapies should be redesigned and clinical trials modified to rapidly identify biomarkers of response and toxicity, including use of co-clinical trials and phase 0 trials'**

David A. Tuveson, MD, PhD, FAACR (past president of AACR)

TTX's FIH Phase 0 study has the potential to:

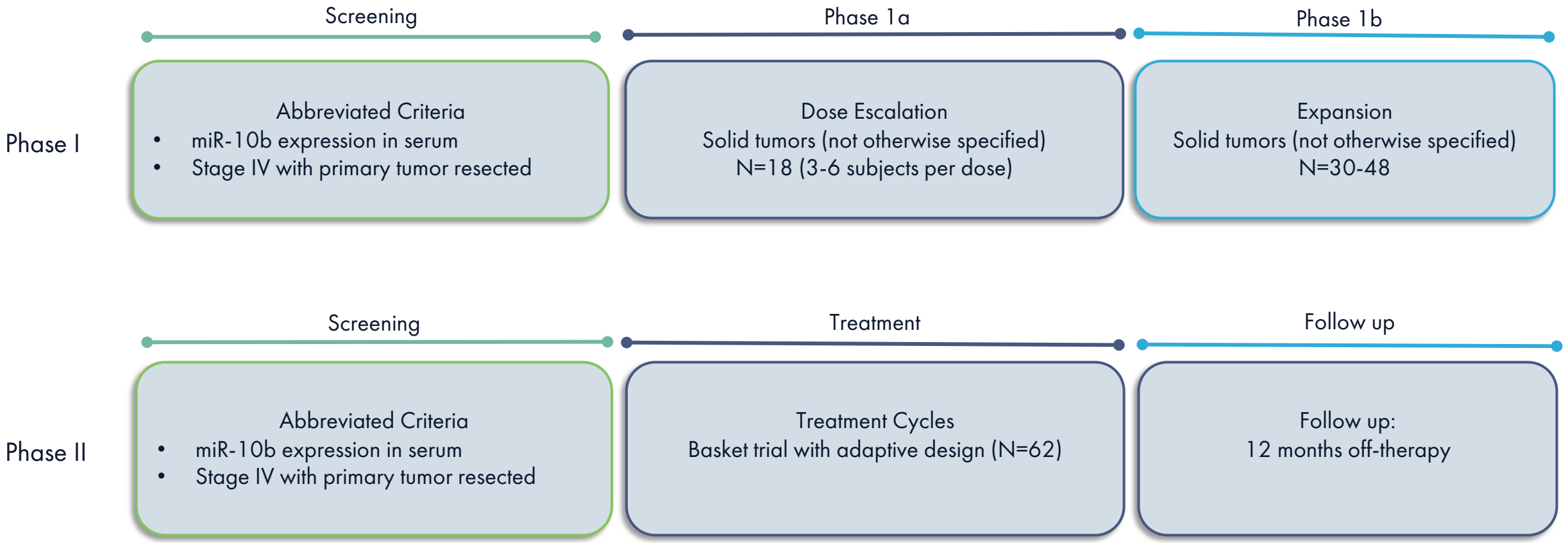


- Demonstrate **quantifiable evidence of delivery of TTX-MC138 to metastatic lesions** in cancer patients with advanced solid tumors
- Inform Ph I/II clinical trials by measuring **pharmacokinetics** & **biodistribution** in vital organs & other tissues
- Extrapolate therapeutic dose level from microdose results for Phase I/II dose
- Validate delivery for the TTX pipeline and open-up additional previously undruggable RNA targets

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

**https://leadingdiscoveries.aacr.org/dr-david-a-tuveson-decoding-a-complex-disease/*

TTX-MC138 Expected Clinical Path for PhI/II



TTX Pipeline

Pipeline Includes Multiple Therapeutic Candidates in Development

Pipeline of First-in-Class RNA Therapeutic Candidates

Drug Candidate	Target	RNA Type	Disease Indication	Discovery	Preclinical	Phase 0	Phase 1	Phase 2	Phase 3
TTX-MC138 (Metastasis focus)	miR-10b	RNAi	Metastatic Breast Cancer						
			**Glioblastoma (GBM); Pancreatic Cancer						
			**SCLC, & Osteosarcoma						
TTX-siPDL1	PD-L1	RNAi	***Pancreatic Cancer						
TTX-MC138Cu^{64}*	miR-10b	RNAi	Metastatic Breast Cancer						
TTX-siLin28b*	Lin28b	RNAi	Pancreatic Cancer						
TTX-RIGA	Multiple	RIGI	Cancer Agnostic						
TTX-CRISPR	Multiple	CRISPR	Cancer Agnostic						
TTX-mRNA	Cancer Vaccine	mRNA	Cancer Agnostic						

* TransCode signed Exclusive Option Agreements with The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, for TTX-siLin28b and ^{64}Cu-TTX-MC138. Under these Options, TransCode has the right to negotiate a license for these candidates with MGH. TransCode's decision will depend on the results of preclinical studies it plans to conduct as shown above. PDAC: Pancreatic ductal adenocarcinoma

** Seeking Orphan designation status

***Received Orphan designation status from FDA

Platform

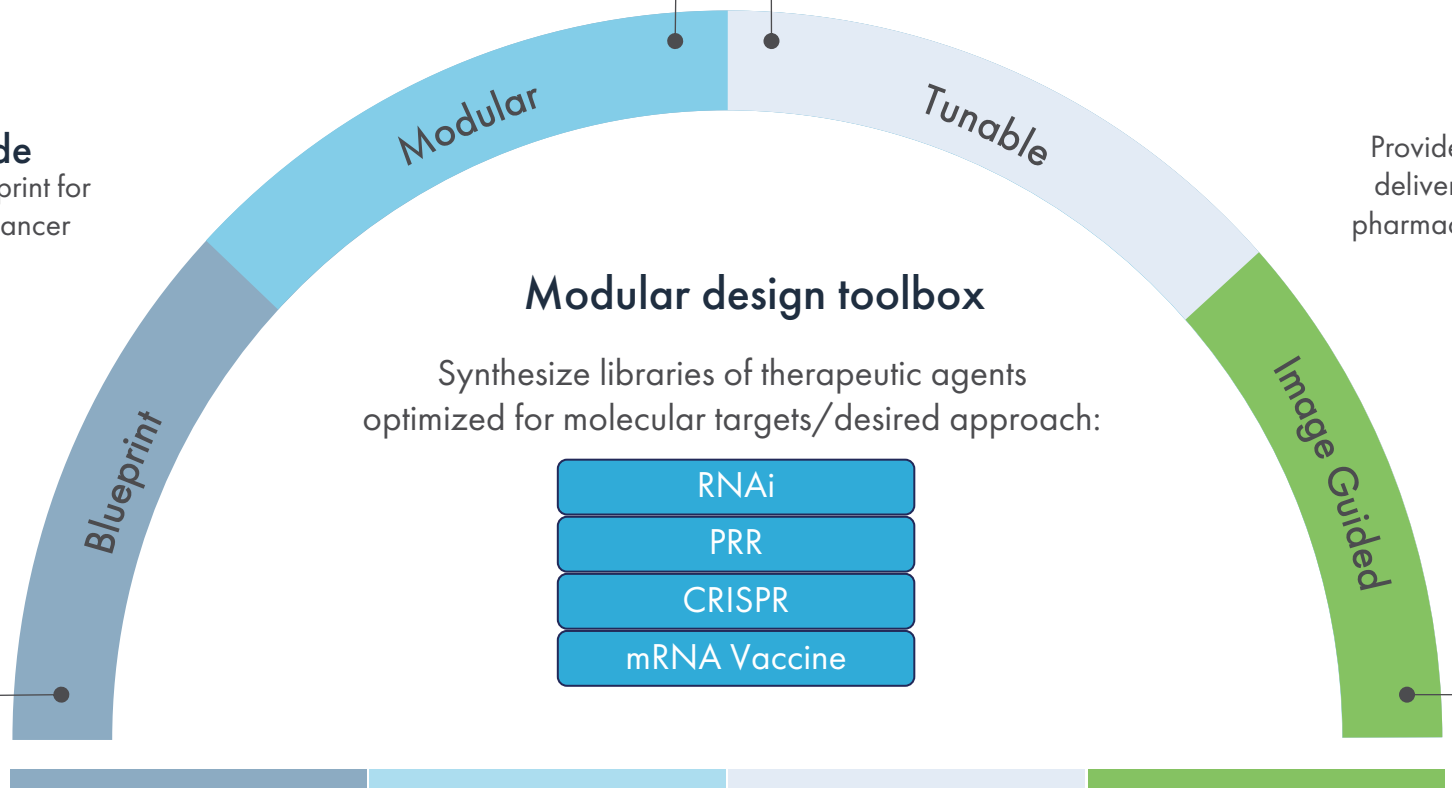
Design Engine to Customize Development of RNA Therapeutics*

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:

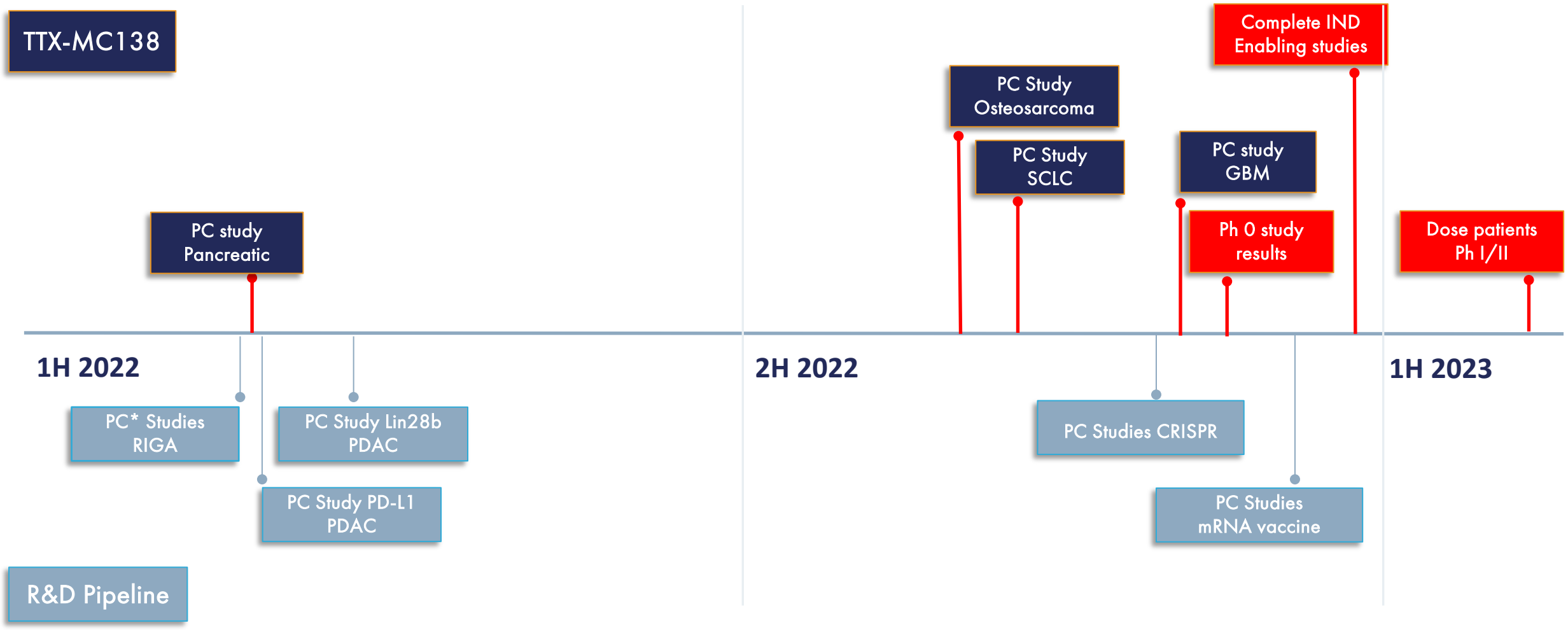
- RNAi
- PRR
- CRISPR
- mRNA Vaccine

*In Oncology and Beyond

Expanding on Strong Pre-Clinical Foundation

- Established Pre-Clinical Results
  - TTX-MC138 MOA is the inhibition of miR-10b, master regulator of metastatic disease in variety of tumor types
    - Well tolerated in pre-clinical studies
    - Pre-clinical POC in aggressive stage II-IV metastatic breast cancer models, solid efficacy results
    - Anticipated participation in one or more of FDA's Expedited Programs
  - Significant results also achieved with siPDL1 and RIGA therapeutic candidates
- Robust Design Engine
  - Opportunity to customize RNA therapeutics for specific tumor indications
- First-in-Class lead therapeutic candidate and pipeline

Timing of Key Milestones



Note: Timelines are estimated and subject to change

* Pre-clinical

2022 Corporate Milestones

Intellectual Property:

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

Regulatory:

- File for Orphan designations

Publications:

- Clinical Applications of non-coding RNA-based Therapies in the Era of Precision Medicine
- Pre-clinical study results for lead candidate in GBM
- Pre-clinical study results for TTX-siPDL1in pancreatic cancer
- Pre-clinical study results 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

Seeking partners to expand:

- Potential of TTX-MC138 lead therapeutic candidate in MBC
- Potential of TTX-MC138 in Colorectal, Pancreatic, Lung, Hepatocellular, Stomach, Ovarian, Glioblastoma, Osteosarcoma, Gastric, Melanoma, Esophageal, SCLC, Thyroid, Endometrial etc.
- Pipeline of therapeutic candidates beyond TTX-MC138
- RNA therapeutic potential outside of oncology

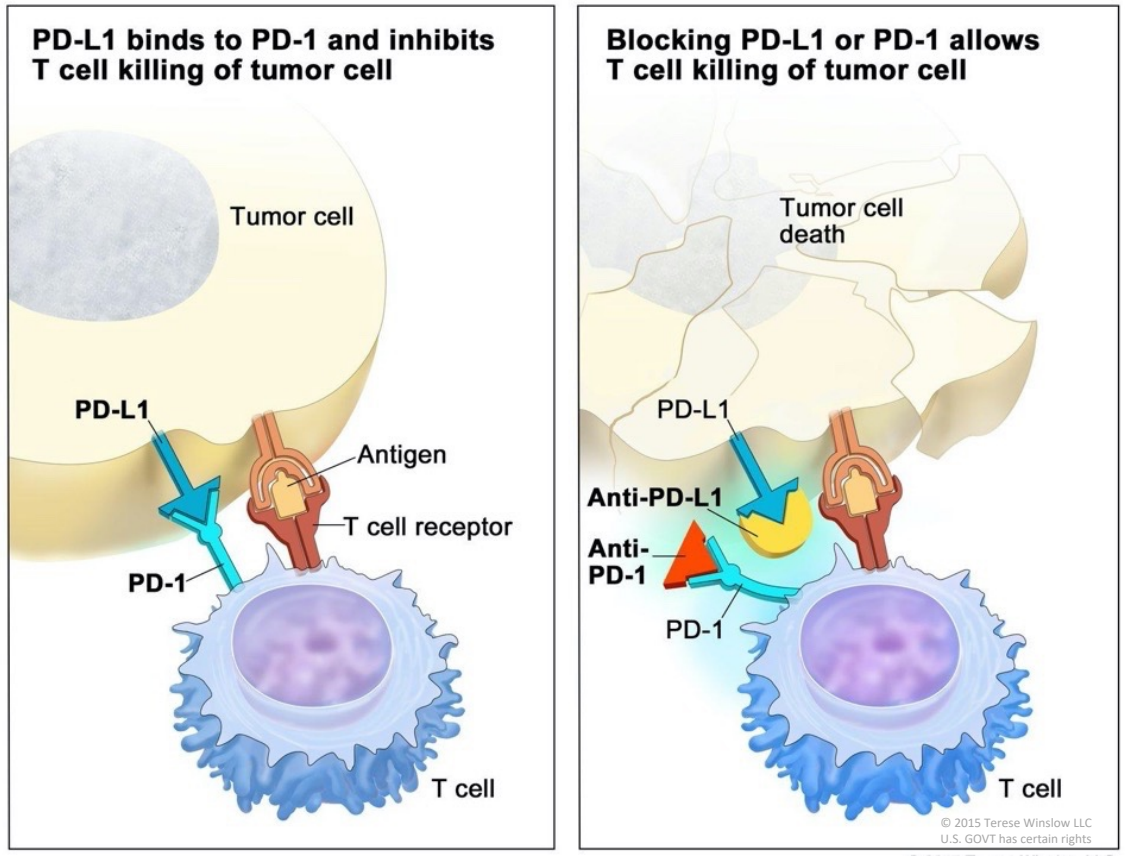
Addendum

Additional Therapeutic Candidates in Development

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

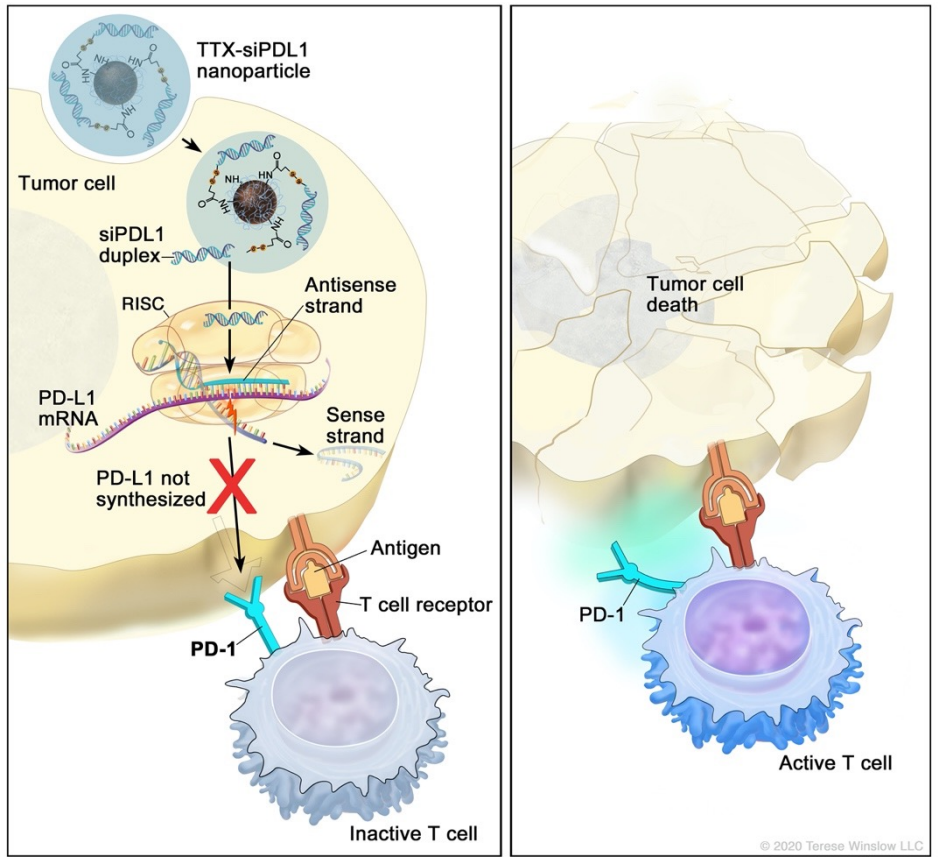
Checkpoint Inhibitors may not be effective in many cancers, including pancreatic cancer:

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



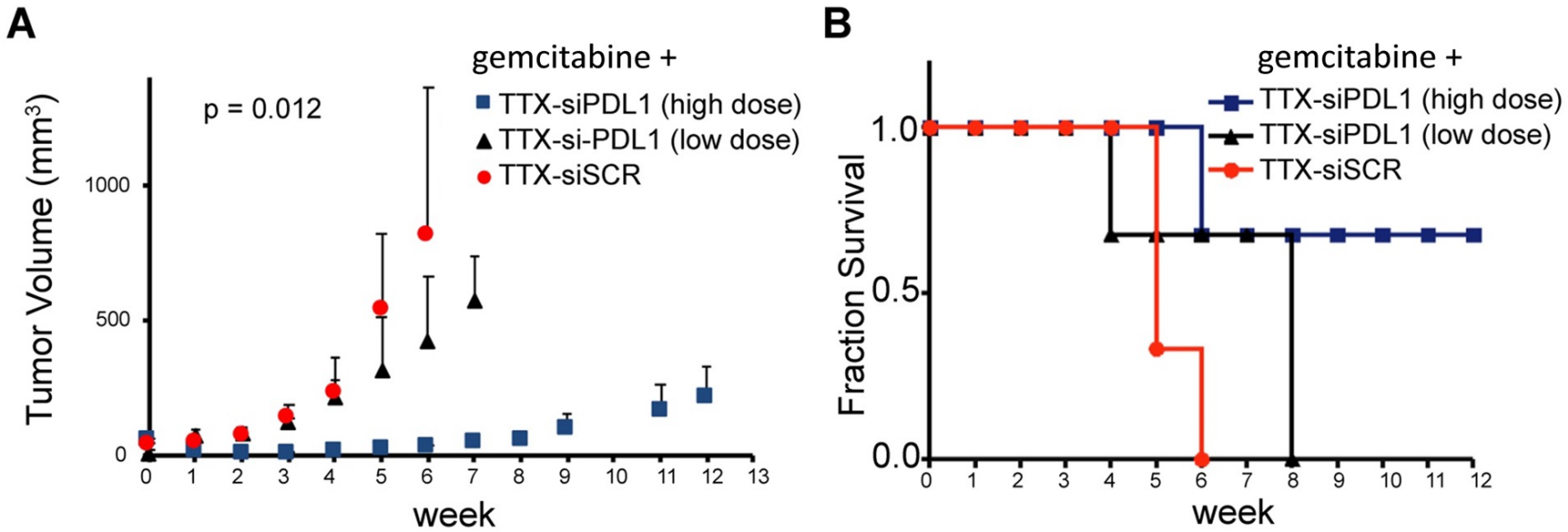
*TTX-siPDL1 – (RNAi) advantages:

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



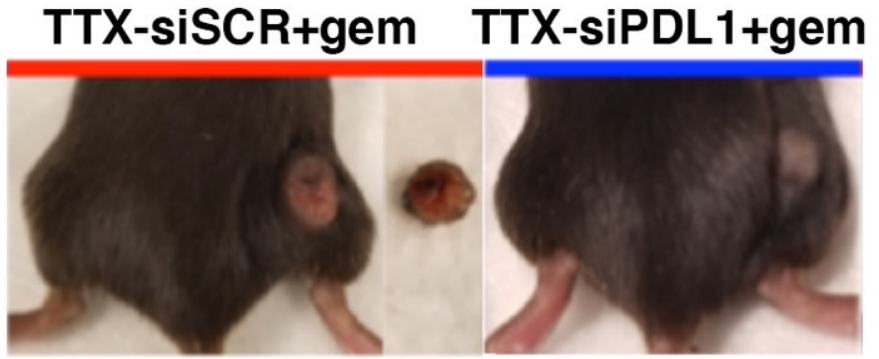
* Received Orphan Designation Status from FDA for Pancreatic Cancer

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

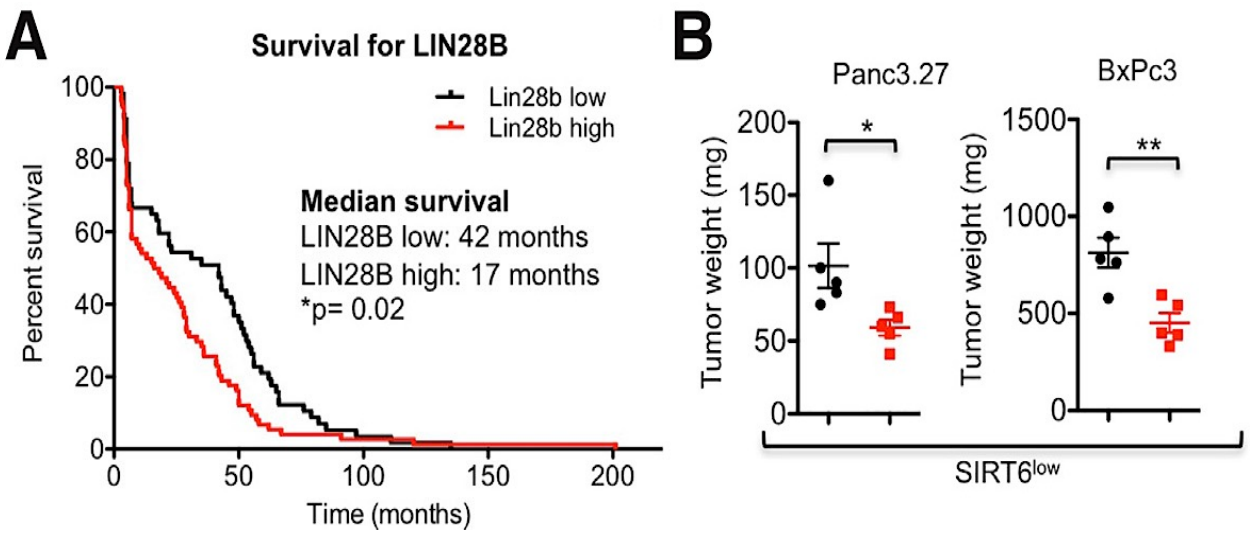
Source: Scientific Reports, 9 (1), 4712 2019

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*)

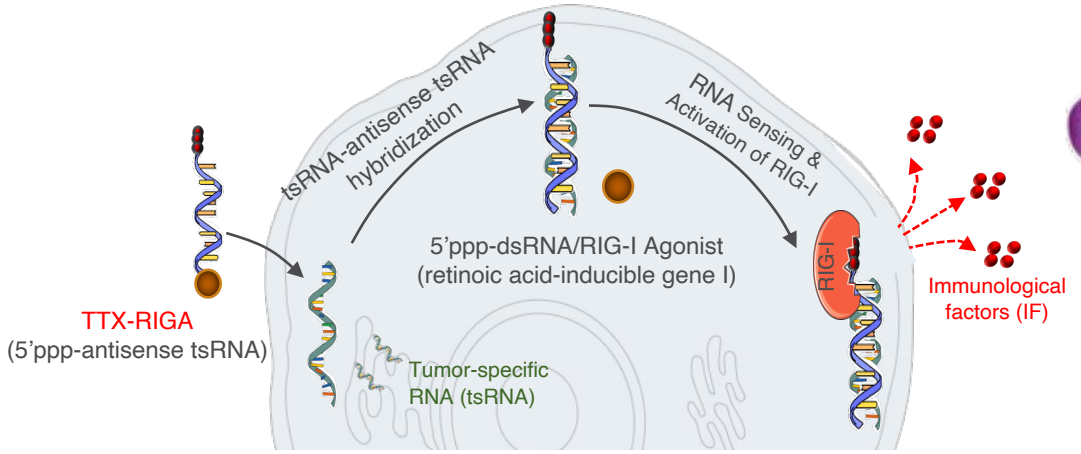
- Lin28b is required for the growth and survival of $SIRT^{low}$ PDAC
- Knocking down Lin28b with both small hairpin RNA (shRNA) and small interfering RNA (siRNA) resulted in potent suppression of cell proliferation and tumor sphere formation
- Knocking down Lin28b inhibited in vivo xenograft growth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

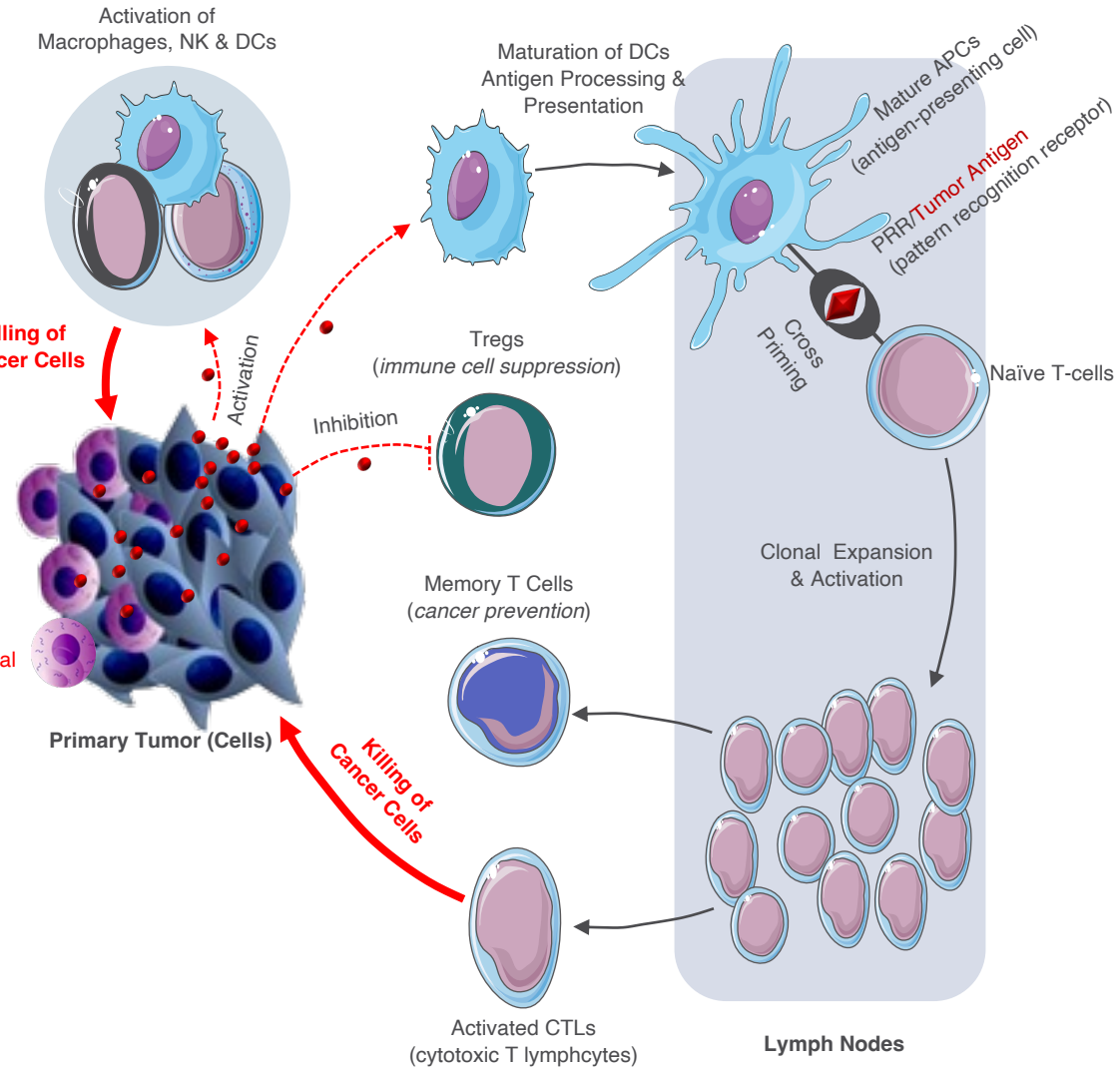
Novel Targeting of Cancer Via RIG-I Signaling Pathway

- 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)

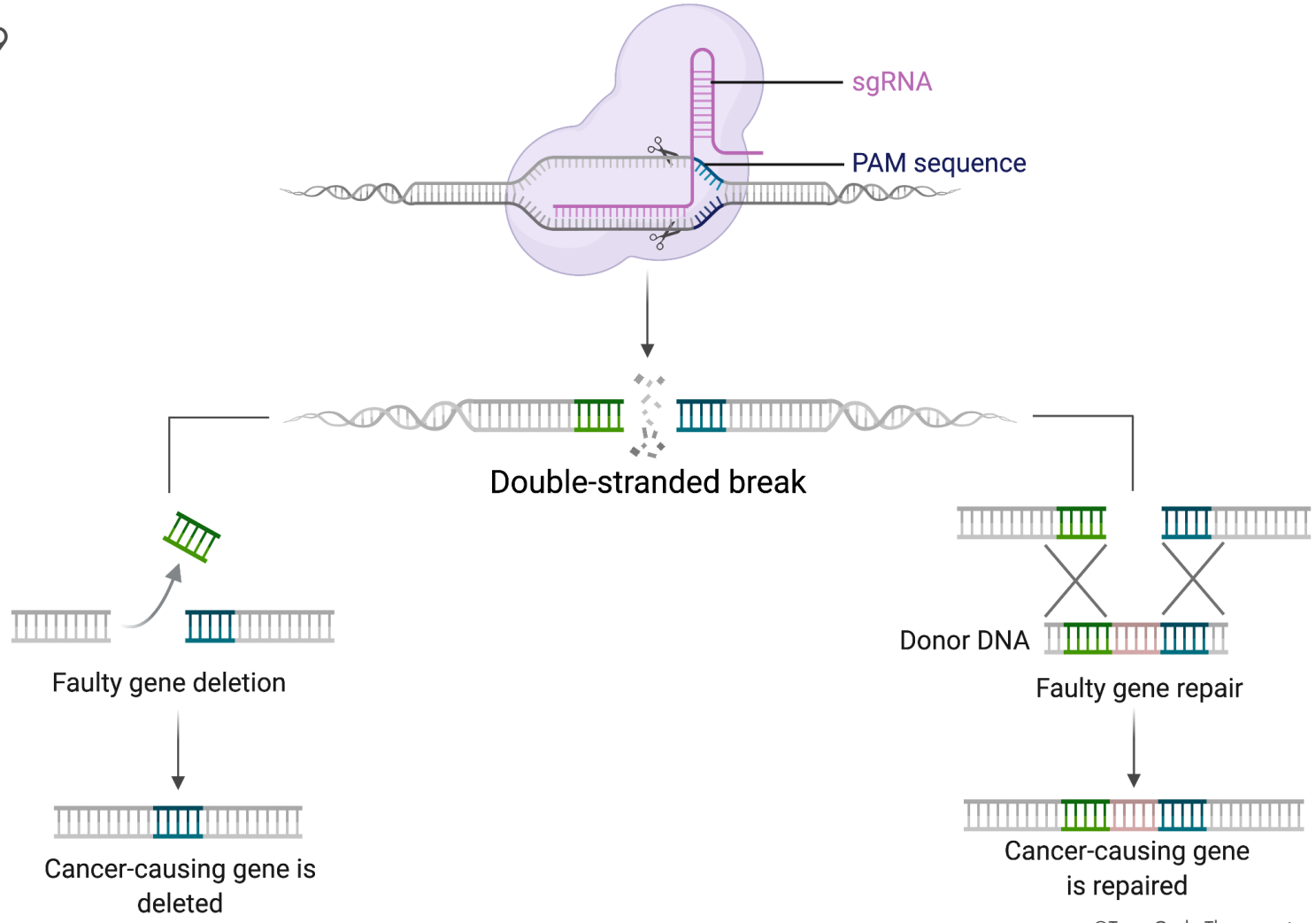


CRISPR/Cas9 Cancer Therapy

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



Created with BioRender.com

mRNA Cancer Vaccine

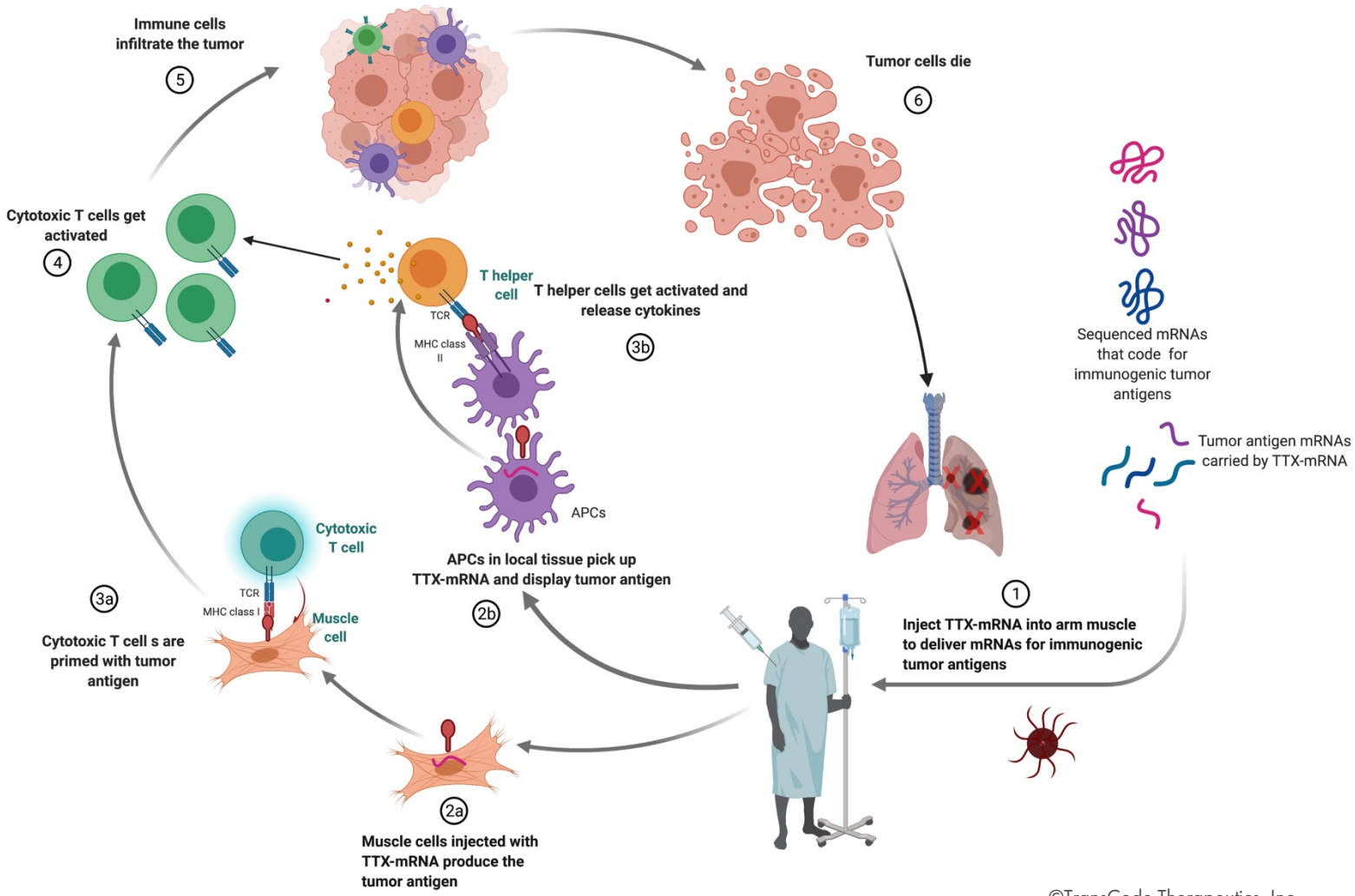
Delivery of TTX-mRNA inside tumor cells to produce an immune response specific to that tumor's immune profile

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



Created with BioRender.com

Our goal is to rapidly advance new scientific discoveries to revolutionize the way cancer is treated to significantly improve patient outcomes

TRANSCODE THERAPEUTICS™