



TRANSCODE

THERAPEUTICS™

**RNA Therapeutics to**  
***Deliver* a Cancer-Free Future**

NASDAQ: RNAZ

October 28, 2024

# Forward Looking Statements

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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 use of words such as "anticipate," "believe," "estimate," "expect," "forecast," "may," "project," "outlook," "should," "will," or other similar words, and include, without limitation, statements regarding the Company's expectations regarding current or future clinical trials, research programs, and financial results including that the Company requires substantial additional capital. Forward-looking statements are based on the Company'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including that clinical trials may be delayed; that reported trial data may be preliminary or interim data which may be superseded by subsequent data obtained from that clinical trial or in connection with other and/or subsequent clinical trials; and that any anticipated meetings with or presentations to the U.S. Food and Drug Administration ("FDA") may be delayed, may not occur at all, or may not result in outcomes that the Company prefers. These and other risks and uncertainties are described more fully in the sections titled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on April 1, 2024, and in other reports filed with the SEC. Forward-looking statements contained in this presentation are made as of the date of this presentation; the Company undertakes no duty to update such information except as required under applicable law.

# TransCode's Innovative Solution to Metastatic Cancer Using RNA

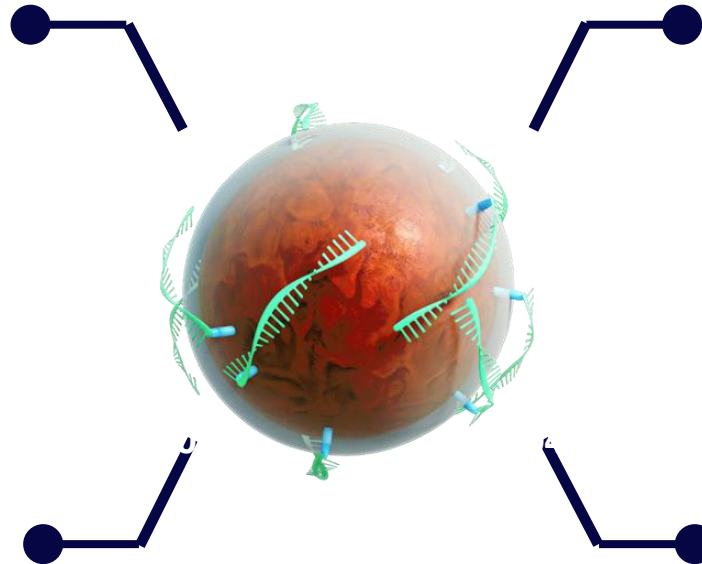


## Unique Approach

- Proprietary nanoparticle delivery platform invented at Harvard Medical School designed to overcome decades of RNA delivery challenges

## Powerful Data

- Compelling data in multiple animal models showed evidence of complete cures of metastatic cancer
- Phase 0 trial in metastatic breast cancer showed delivery to clinical metastases and PD activity, even at microdose



## Lead Candidate

- TTX-MC138 targets miR-10b, an important oncogene in metastatic cancer
- Currently in Phase I/II clinical trial

## Corporate Strengths

- Robust IP: 10 patents in 5 patent families
- Several industry collaborations in place
- Highly experienced management team





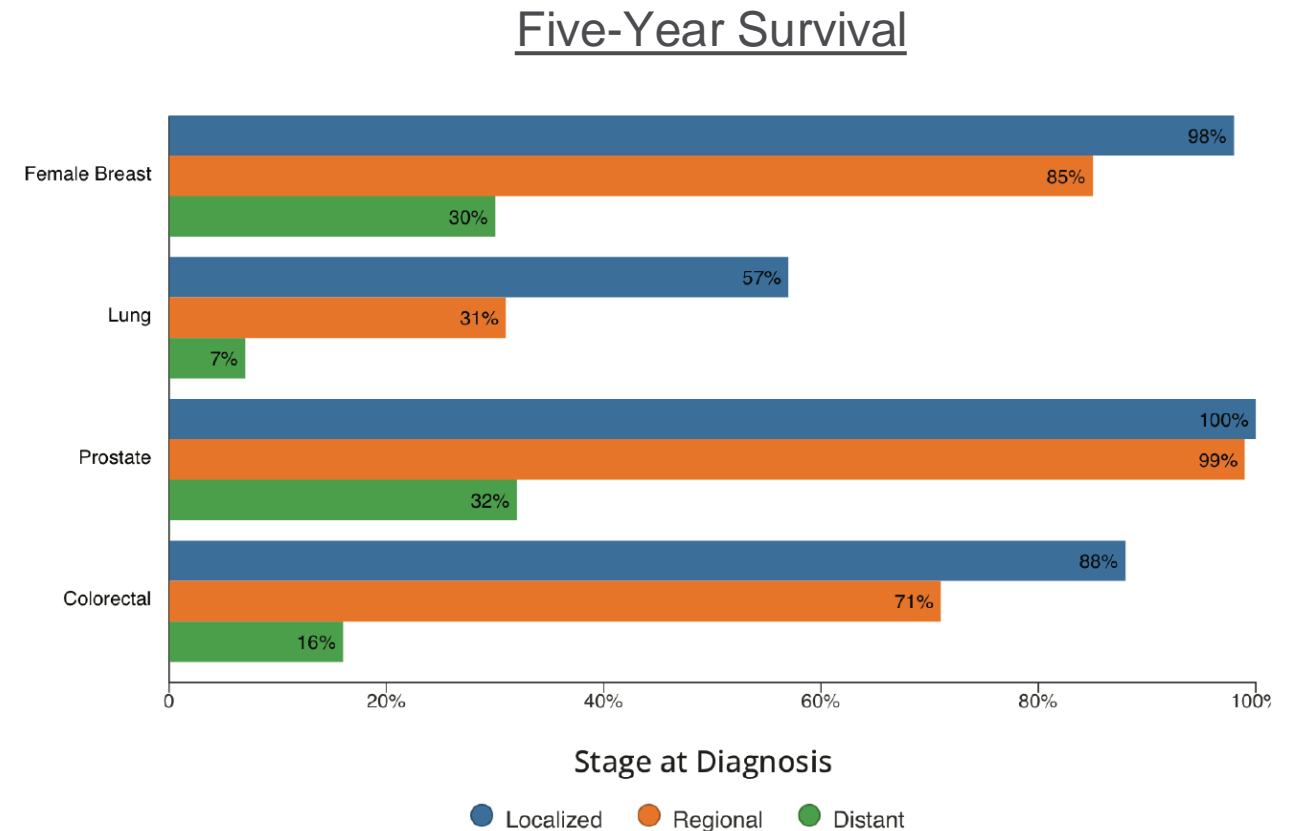
# Critical Need for An Effective Therapy Against Metastatic Cancer



Metastatic cancer is essentially incurable

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

~\$137B global market by 2032



# Delivery Challenges / Opportunities

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About 80% of currently known oncology targets are undruggable using monoclonal antibodies (mAbs) and/or small molecules

Engaging these targets using RNA/DNA is possible, provided that the RNA/DNA molecules can be **delivered** to cancer cells in humans

TransCode's proprietary delivery platform addresses the challenge of delivering RNA/DNA molecules to cancer cells

TransCode's delivery platform is based on tunable chemistry and employs a design engine to build RNA/DNA drugs according to desired specifications

By enabling delivery of RNA/DNA to cancer cells, TransCode's delivery platform could revolutionize cancer treatment by opening up a vast pipeline of new anti-cancer drugs



# TransCode's Tunable TTX Delivery Platform

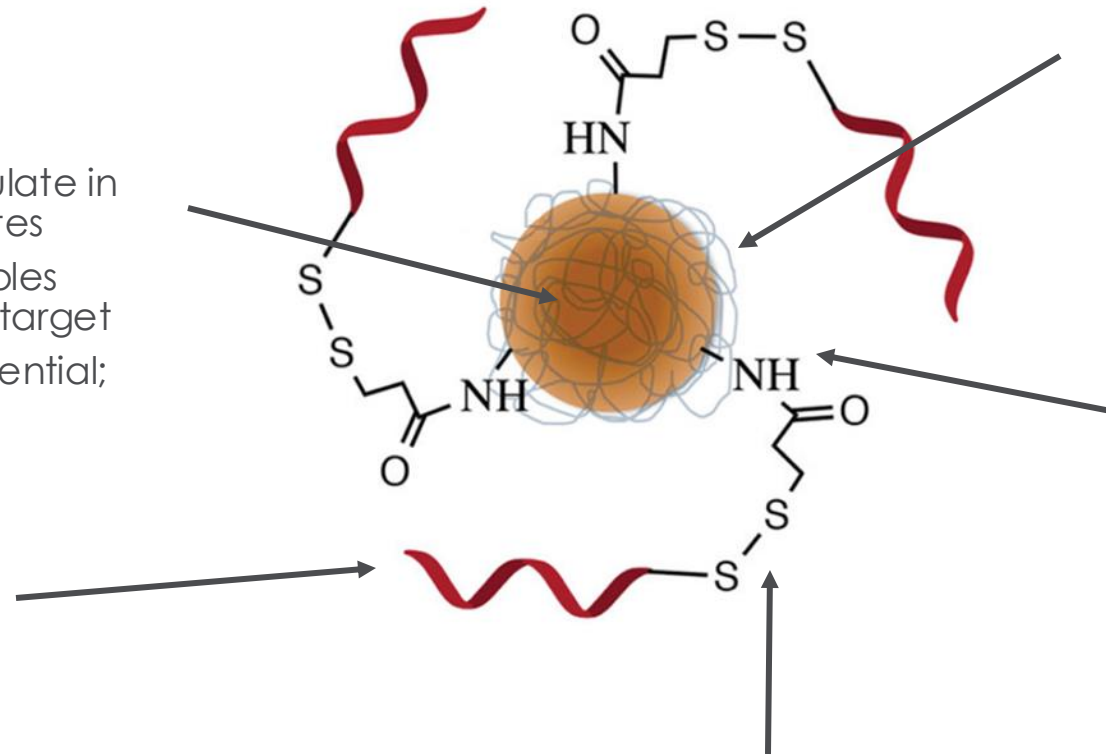


## Tunable Nanoparticle Platform

- Size customizable according to desired pharmacokinetics
- 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

## Range of Payloads

- Nucleic acids
- Proteins
- Peptides
- Radionuclides
- Small molecules



## Customizable Coating

- Stabilizes nanoparticles
- Protects cargo from degradation
- Promotes tumor uptake and entrapment inside tumor cells
- Allows control over drug pharmacokinetics

## Range of Functional Groups

- Enable payload linkage to the nanoparticle
- Allow control over payload density and type of chemistries for payload binding
- Allow control over physicochemical properties and pharmacokinetics

## Smart Release Technology

- Allows payload to bind to/release from carrier according to specifications

# Multiple First-in-Class RNA Therapeutic Candidates



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	Cancer Agnostic						
TTX-CRISPR	Internal	CRISPR (Cas9)	Cancer Agnostic						
TTX-BEC	Akribion Genomics	CRISPR (BEC)	Cancer Agnostic						
Targeted TTX- RNA	Debiopharm	RNA	Cancer Agnostic						
TTX- mRNA	Undisclosed	mRNA	Cancer Agnostic						

\* Received Orphan designation status from FDA



# Lead Candidate: TTX-MC138

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

Target: 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 - Scans

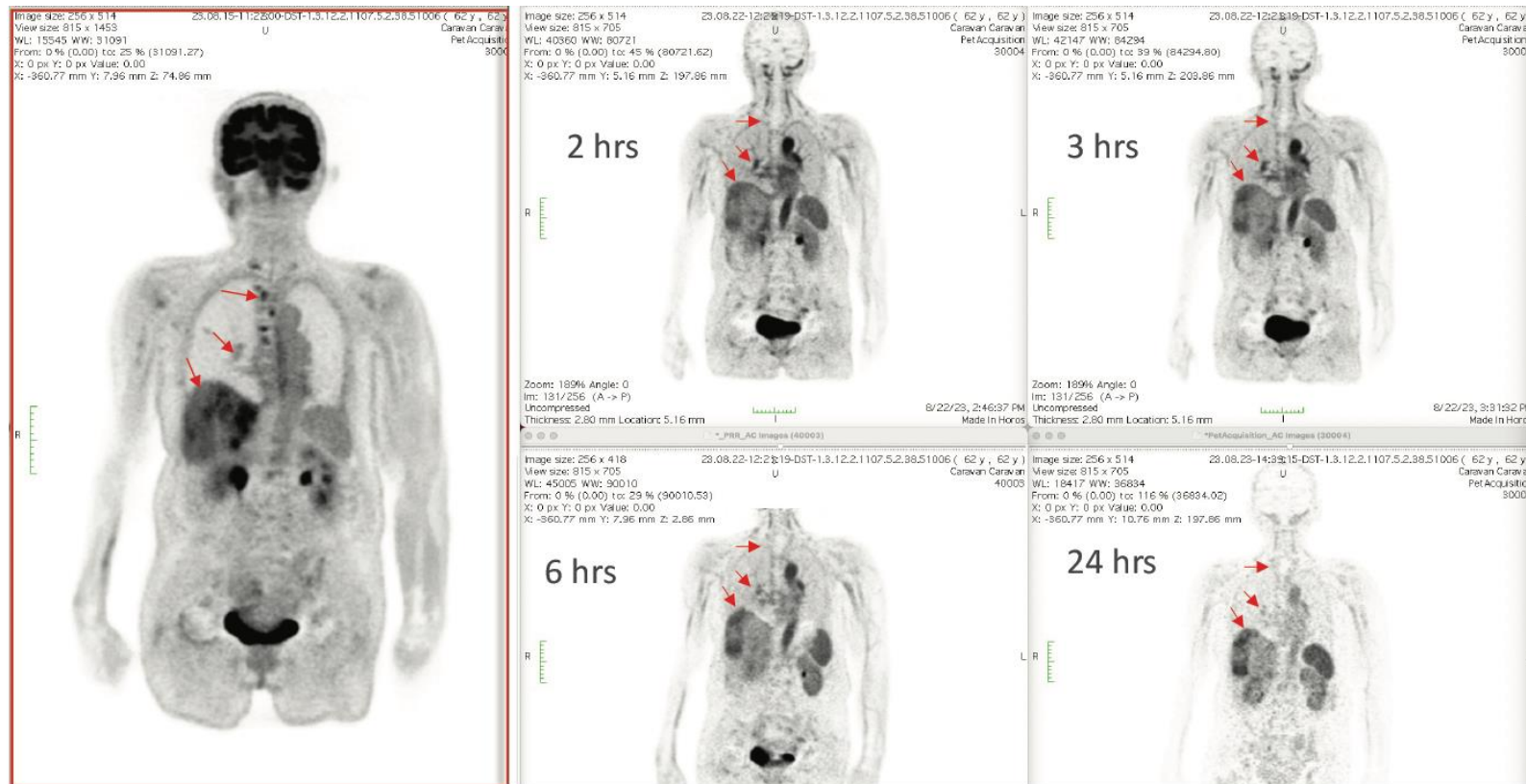


## PET-MRI To Determine Drug Delivery

### FDG PET-MRI

### 64Cu-TTX-MC138 PET-MRI

- Female, Stage IV, metastatic breast cancer. Metastatic sites: bone, liver, lungs
- Before dosing with TTX-MC138, FDG PET-MRI was used to locate metastatic lesions (*red arrows in larger image*)
- PET/MRI at 2, 3, 6 and 24 hours post-dosing was used to detect presence of TTX-MC138 (*red arrows in small images*)

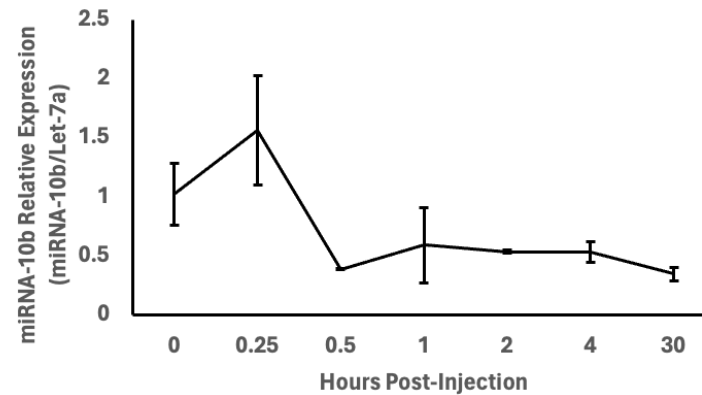


Dynamic Imaging and PD Activity Data

# Phase 0 Preliminary Results - Blood



miRNA-10b Inhibition by Radiolabeled TTX-MC138  
in Patient Blood



qRT-PCR To Determine Drug Functionality

## TTX-MC138 Preliminary Results

- Accumulation in the metastatic lesions (*red arrows in scans*)
- Drug functionality/target engagement (*patient blood*)
- No safety issues and absence of any allergic hypersensitivity related adverse events

# TTX-MC138 Phase I/II Trial Design



TTX-MC138 Phase I/II clinical trial designed to:

- Assess safety
- Determine recommended Phase 2 study dose
- Early tumor activity
- Results in different types of metastatic tumors

## Screening

Advanced Solid Tumors

## Phase 1a

Escalating Dose Levels  
Indication: All comers  
Design: Bayesian Optimal Interval (BOIN)  
N ≤ 32

## Phase 1b

Dose Expansion  
Up to 3 cohorts; indications TBD.  
Design Scenario: dose level and  
schedule pending Ph 1a results

# Enrolling TTX-MC138 Phase I/II Trial

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Design: 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

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

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

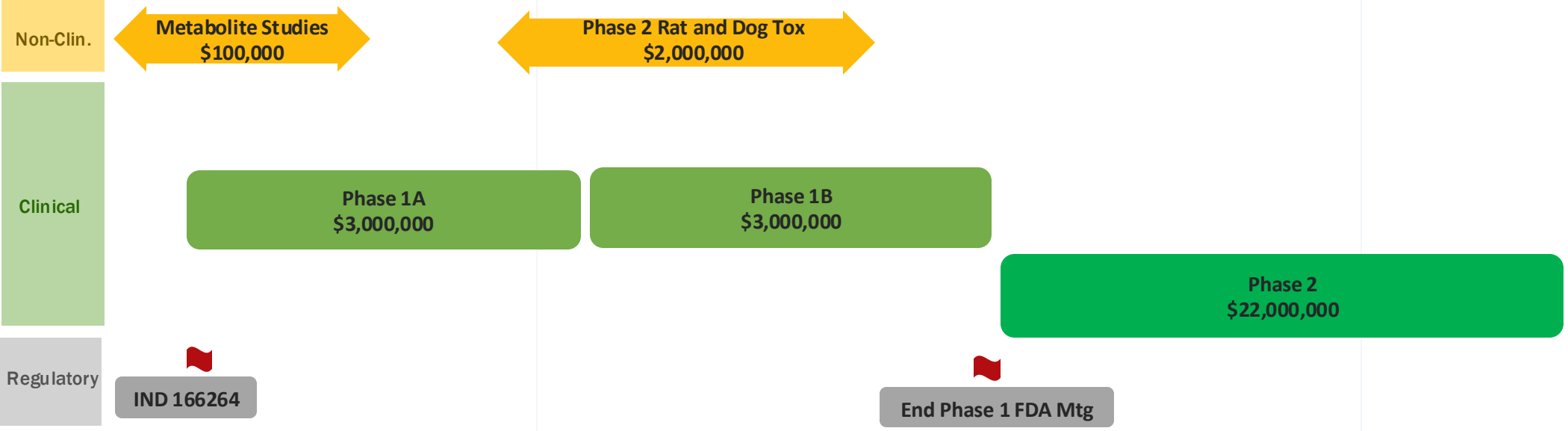
Dosing Scheme: Up to four dose levels planned for evaluation

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

# TTX-MC138 Clinical Program Overview



2024	2025				2026				2027				2028				2029			
Q1-4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4



Costs are direct costs of clinical-related costs; do not reflect cost of oOperations



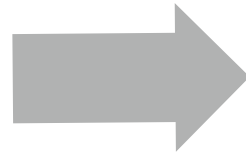


# Recent and Expected Milestones



**2024**

- ✓ TTX-MC138 IND
- ✓ TTX-MC138 Phase 0 completion
- ✓ TTX-MC138 Phase 1a initiation
- ✓ Second NIH Grant (\$2M)
- ✓ Debiopharm Partnership



**2025**

- TTX-MC138 Phase 1a completion
- TTX-MC138 Phase 1b initiation
- TTX-MC138 Phase 0 publication
- TTX-MC138 Partnership
- TTX Partnership(s)
- Grants

# Capitalization



Source of Capital	Amount
Seed Capital (Angel investors)	\$2,240,000
SBIR Grants	4,309,000
IPO (Net Proceeds)	25,400,000
Equity Financings (2023, 2024) (Net Proceeds)	24,107,000
<i>Total</i>	\$56,056,000

NASDAQ: RNAZ	Sept 30, 2024
Common Stock	17,265,658
Warrants (WAEP/Sh \$2.49)	12,231,491
Options (WAEP/Sh \$2.70)	1,935,813
<i>Total</i>	31,432,962

# 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

## Independent Directors

## Key Advisors



Tom Fitzgerald,  
MBA  
Interim CEO,  
CFO



Zdravka  
Medarova, PhD  
Founder/Chief  
Scientific Officer



Susan Duggan,  
RN, MBA  
Sr. VP of  
Operations



Tania  
Montgomery,  
VP Business  
Development



Philippe Calais,  
PhD  
Chairman



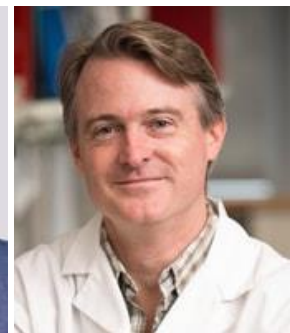
Magda  
Marquet, PhD  
Director



Erik Manting,  
PhD  
Director



Keith  
Flaherty, MD  
Advisor



Frank Slack,  
PhD  
Advisor



Lubo  
Nechev, PhD  
Advisor





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Back-up Slides

# Value-Generating Strategic Collaborations



Candidate	Partner	Program
Targeted TTX-RNA	Debiopharm	Testing in vitro delivery of RNA inside tumor cells
TTX-mRNA	Undisclosed	mRNA delivery to tumors
TTX-CRISPR (BEC)	Akribion Genomics	Development of cell-killing G-dase E, a Class 2 CRISPR nuclease, with TransCode's TTX nucleic acid delivery platform
TTX-siRNA	In Discussion	Tumor-targeted siRNA delivery
TCD-miR-10b	LabCorp	Developing assay for clinical measurement of miR-10b in patient samples from 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



# Patents and Applications



Cover both composition of matter and methods claims

Technology	Geography	Expiration	Patents/Applications	Notes
TTX for Payload Delivery	US, EU, CA, CN, KR	2039	WO2021/113829	Payload delivery
Nanosensor	75% of World	2043	US10,086,093; EP 2 961 386	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	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	Delivery of siRNA