

Clinical Stage Platform Delivery Company Overcoming Intractable Problems in Oncology and Beyond

TRANSCODE

THERAPEUTICS™

NASDAQ Symbol: RNAZ

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# **Cancer Market**

### Problem Critical Need for New Cancer Therapies Especially Targeting Metastasis

- Oncology Market Size to Hit \$581.25 Billion (USD) by 2030
- Global new cancer cases are expected to rise by 47% from 2020 to 2040
- Metastasis Reduces 5-year Survival
- 90% of Cancer Deaths Due to Metastasis\*
- Our lead therapeutic candidate TTX-MC138 has the potential to treat cancer patients in 19 different solid tumor indications
- Checkpoint Inhibitors currently account for most of the cancer treatment revenue (top 5 drugs = \$50 B in annual sales) yet only ~ 3% of patients positively responding

Metastasis: Cancer that spreads from organ of origin to other places in the body

18.1 Million Cancer Patients Newly Diagnosed Annually



Other therapies (Chemo etc)





TransCode is focused on creating new molecular therapies using its platform delivery system with the goal to achieve long-term survival for cancer patients



| Value<br>Proposition                 | <ul> <li>Clinical stage company with highly differentiated technology with goal to achieve long-term survival for cancer patients</li> <li>Proprietary delivery platform designed to overcome the major challenges with therapeutic delivery</li> <li>Potential for broad applicability across multiple targets and cancer indications</li> <li>Complete regression of established metastases in preclinical models of breast and pancreatic cancer with lead candidate</li> <li>Proof of concept demonstrating successful delivery of multiple therapeutic modalities inside tumor cells</li> <li>Extensive IP portfolio</li> </ul>   |
|--------------------------------------|--|
| Major<br>Differentiating<br>Features | <ul> <li>Proprietary delivery platform:</li> <li>✓ Tunable chemistry optimized for functionalization against relevant documented oncology targets</li> <li>✓ Size and charge optimized for stability, long circulation, and optimal PK and tissue distribution</li> <li>✓ Favorable safety profile with similar nanoparticles used in cancer imaging and treatment of iron deficiency anemia</li> <li>✓ Image-capable platform via MRI provides visual confirmation and quantification of delivery</li> <li>✓ Enables the endosomal/lysosomal escape via the proton sponge effect for cytosolic delivery</li> <li>✓ Superior stability, amendable for lyophilization (most payloads) avoiding cold chain logistics extending shelf life potential</li> </ul> |
| Unmet<br>Need                        | <ul> <li>9.9 million people died of cancer in 2020 and over 90% of those cancer deaths are attributable to metastatic disease*</li> <li>Current treatments serve a mostly palliative role in advanced stages of disease</li> </ul>   |
| Market<br>Opportunity                | <ul> <li>Metastatic cancer market to reach \$111 billion by 2028<sup>**</sup></li> <li>Undervalued therapeutic assets with potential for significant return on investment</li> <li>Average M&amp;A deal value for Phase I oncology companies: \$862 million<sup>***</sup></li> </ul>   |

## Milestones Achieved Milestone Achievements

TransCode achievement of key milestones since inception



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# **Expanding Delivery Platform**

Advancing First-in-Class Therapeutics

#### Delivery Platform Proprietary Platform with Potential to Deliver a Broad Array of Therapeutics







# Persistent Therapeutic Delivery Challenges:

- Delivery of RNA therapeutics to oncology targets
- Precise genome editing using systemically-administered genome editing tools (e.g., CRISPR)
- Delivery of potent and safe mRNA vaccines
- Endosomal escape pathways that enable intracellular delivery of molecular therapeutics

We believe overcoming the challenges of delivery would represent an important step in unlocking therapeutic access to a variety of documented targets involved in a range of cancers and beyond Our therapeutic delivery strategy employs nanoparticles extensively used in imaging that have been <u>repurposed</u> and <u>optimized</u> to efficiently deliver payloads to oncology targets

#### Preclinical evidence TTX has overcome delivery challenges:

- Superior stability, amenable for lyophilization (most payloads) avoiding cold chain logistics extending shelf life potential
- Enables the endosomal/lysosomal escape via the proton sponge effect for cytosolic delivery
- Unique magnetic property able to confer numerous multimodal therapies/theranostics
- Size & surface chemistry highly tunability able to access desired tissue target (e.g., TME), enormous flexibility for target delivery
- Simplicity and cost-effective production
- Safety biodegradability and low immunogenicity
- Readily adaptable for stabilizing various types of payloads (including labile ones)





Competitive TTX Delivery System Comparison to Lipid Nanoparticles

### -Sequence

ANS

### Relative Comparison of LNP & TTX Delivery Characteristics



Stability Delivery efficiency Safety Endosomal escape/cytosolic delivery Target engagement Tunable surface chemisty Image capable

#### LNP = Lipid nanoparticles TTX = Dextran coated iron-oxide nanoparticles

### Competition & Unique Particle Size Coupled with Exceptional Safety





### Competition & Differentiation Summary

- TTX particle size allows for a long circulation time & efficient accumulation in the tumor while minimizing kidney & liver clearance
- Competitors' lipid nanoparticles carry a risk of immunogenicity that is avoided with TransCode's iron oxide particles
  - Iron oxide nanoparticles verified safe after decades of use as an imaging agent & FDA-approved treatment for iron deficiency anemia
- Dextran coating reduces solution aggregation & improves stability

TransCode's Iron Oxide Nanoparticle Optimized for Delivery to Oncology Targets



Pipeline

### Pipeline Advancing a Pipeline of First-in-Class RNA Therapeutic Candidates



| Drug<br>Candidate | Target   | Туре          | Disease Indication                               | R&D | Preclinical | IND Enabling | Phase O | Phase 1 | Phase 2 | Phase 3 |
|-------------------|----------|---------------|--|-----|-------------|--------------|---------|---------|---------|---------|
|                   |          |               | Metastatic Cancer                                |     |             |              |         |         |         |         |
| TTX-MC138         | miR-10b  | RNAi          | * *Glioblastoma (GBM);<br>* * *Pancreatic Cancer |     |             |              |         |         |         |         |
|                   |          |               | * * SCLC, & Osteosarcoma                         |     |             |              |         |         |         |         |
| TTX-siPDL1        | PD-L1    | RNAi          | * * * Pancreatic Cancer                          |     |             |              |         |         |         |         |
| TTX-siLin28b*     | Lin28b   | RNAi          | Pancreatic Cancer                                |     |             |              |         |         |         |         |
| TTX-RIGA          | Multiple | RIGI          | Cancer Agnostic                                  |     |             |              |         |         |         |         |
| TTX-CRISPR        | Multiple | CRISPR (Cas9) | Cancer Agnostic                                  |     |             |              |         |         |         |         |
| TTX-CRISPR        | Multiple | CRISPR (BEC)  | Cancer Agnostic                                  |     |             |              |         |         |         |         |
| TTX-mRNA          | Vaccine  | mRNA          | Cancer Agnostic                                  |     |             |              |         |         |         |         |

\*\* Seeking Orphan designation status

\* \* \* Received Orphan designation status from FDA

Shaded portions indicate for external partner development

<sup>\*</sup> TransCode signed Exclusive Option Agreements with The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, for TTX-siLin28b and <sup>64</sup>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.



# Lead Candidate - TTX-MC138 Targeting Mechanisms of Cancer Progression in Multiple Cancer Indications

## Validated<br/>BiomarkermicroRNA-10b is a Unique, Well Documented Biomarker of Metastasis



Clinical evidence demonstrated in >700 peer-reviewed publications over the last ten years

- Biomarker of cancer progression, higher cancer risk and poor survival outcomes
- Linked to metastatic progression in multiple cancer indications including Breast, Colorectal, Pancreatic, SCLC, Osteosarcoma, Liver and other rapidly proliferating cancers like GBM etc.



miR-10b upregulation in primary tumor cells leads to metastatic tumor cell formation, detachment from the primary tumor and migration to other areas of the body forming new metastases

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





TTX-MC138 delivered to tumor cells in metastatic lesions to engage miR-10b

miR-10b inhibition has been shown to activate miR-10b downstream apoptotic pathway

miR-10b inactivation has been shown to lead to tumor cell death and elimination of existing metastases

#### Pre-Clinical POC Prevention of Metastatic Breast Cancer





\* MN-anti-miR10b = TTX-MC138 MN-scr-miR = inactive TTX-MC138

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

## Pre-Clinical POC Elimination of Existing Metastases in Triple Negative Breast Cancer





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

Study design: mice (n=35) implanted with MDA-MBA-231 -luc-D3H2LN

## TTX-MC138 eliminated pre-existing local metastases (lymph node metastases) in <u>100% of the animals</u> treated



weeks

Therapy stopped

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

Study design: mice (n=39) implanted with 4T1-luc2 cells

# TTX-MC138 eliminated pre-existing distant metastases (cancer spread to distant organs like lung metastases) in <u>65% of the animals</u> treated

\*TNBC, Triple Negative Breast Cancer

#### TTX-MC138 Preliminary Results of Pre-Clinical Efficacy in Pancreatic Cancer Model\* Pre-Clinical POC





PBS \_ Gemcitabine TTX-MC138 15 20 25 Weeks



- Results: 40% of animals treated with TTX-MC138 showed 100% regression of disease without recurrence during the length of the study (20wks)
- qRT-PCR shows target engagement and the potential to use miR-10b expression in serum as a biomarker of therapeutic success



# Lead Therapeutic Candidate TTX-MC138 Clinical Path Forward

First In Human (FIH) Phase O Study Phase I/II Clinical Trial

#### Regulatory Strategy First-in-Human Phase O Clinical Trial – <sup>64</sup>Cu-TTX-MC138

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- Demonstrate quantifiable evidence of delivery to metastatic lesions in cancer patients with advanced solid tumors
- Validate delivery for the TTX pipeline and open-up additional previously undruggable RNA targets



- Primary Endpoints:
  - PET/MRI pre and post therapy to visualize and quantify delivery of radiolabeled TTX-MC138
  - Demonstrate delivery of <sup>64</sup>Cu-TTX-MC138 to metastatic lesions

- Secondary Endpoints
  - Inform Phase I/II dose level from microdose results
  - Inform Ph I/II clinical trials by measuring pharmacokinetics & biodistribution in vital organs & other tissues
- Exploratory Objectives:
  - Measure microRNA-10b expression in patient serum pre and post dose

Received Written Authorization from FDA and IRB Approval to Proceed



|                    | Study Summary  |   |  |  |  |
|--------------------|--|---|--|--|--|
| Proposed Trial des | sign   |   |  |  |  |
| Screening          |  | Phase 1a  | Phase 1b   |  |  |
| Ab<br>• n<br>• S   | breviated criteria<br>nicroRNA-10b expression in serum<br>Stage IV with primary tumor resected | Escalation (SAD and MAD)<br>Solid tumors (not otherwise specified)<br>Bayesian Optimal Interval Design (BOIN)<br>N=12 (4 subjects per dose) TBD<br>Design Scenario: Adaptive/All comers | Expansion<br>All-comers that meet inclusion criteria<br>Expansion at MED dose N=18<br>Design Scenario: All comers, one or three<br>tumor types |  |  |

- Phase 1a objective: Safety assessment (3 Dose Levels)
  - Secondary objectives: Confirm delivery to tumor site & evaluate pharmacokinetics, pharmacodynamics
- Phase 1b objective: Exploratory Clinical Pharmacology ( Dose Level)
- Secondary objectives: ORR according to investigator's assessment, duration of response, safety and additional pharmacokinetic & pharmacodynamic evaluations
- Multi-center trial; up to 50 subjects
- Follow up: Up to 6 months

- Critical Inputs Being Evaluated:
- Dose Rationale: Non-clinical data, NHP data, Physiologic PK Model
- Schedule: Tox study design gives us coverage of up to two doses, one week apart.
  - FDA may allow for more frequent dosing given late-stage oncology (Pre-IND question)
  - $_{\circ}~$  FDA may require more tox data for longer duration of dosing
- Indications: How do different tumors react to dose and/or schedule?

Clinical trial design assesses safety & RP2D\* and potential indication of clinical pharmacology (target inhibition)



# **External Partnership Development** Out-licensing/Partnering Opportunities

### Pipeline R&D Pipeline Market Opportunity





Growth Market Reports January 2023; Emergen Research 2021; KD Markets Insight 2023; Allied Market Research 2023; Research Reports World 2023; Coherent market insights 2023; Research and Markets 2023 26

#### Product Development Historical Timeline for Product Development



2023

Expanding delivery capability includes CRISPR-based genome editing and mRNA vaccines as well as other molecular therapies outside of RNA



# Partnering Partnership Progress



| Product           | Potential<br>partner(s)     | Program progress to date  |
|-------------------|-----------------------------|---|
| TTX-CRISPR (BEC)  | Akribion<br>(BRAIN Biotech) | Optimizing in vitro POC then move into animals  |
| TTX-CRISPR (Cas9) | TBD                         | In vitro success – optimizing for next steps and animal study   |
| TTX-siRNA         | 2                           | Potential pilot studies demonstrating tissue specific targeted delivery                                     |
| mRNA Vaccine      | TBD                         | Successful in vitro delivery of mRNA inside tumor cells; next step is optimizing for animal study POC       |
| Radio-TTX-miR-10b | TBD                         | Entering Phase O First in Human clinical trial  |
| TCD-miR-10b       | LabCorp                     | Developing assay with partner for clinical measurement of miR-10b in patient samples for clinical trials    |
| TBS-Nb            | TBD                         | Provisional patent filed (covering other molecular therapies delivery including proteins, nanobodies, etc.) |

Corporate Capitalization



| Sources of Capital                | Amount       | NASDAQ Symbol: RNAZ              | Shares     |  |
|-----------------------------------|--------------|----------------------------------|------------|--|
| Seed Capital<br>(Angel investors) | \$2,240,000  | Common Stock<br>(Mar. 31, 2023)  | 15,823,534 |  |
| SBIR Grant                        | 2,300,000    | Shares under S-3<br>(April 2023) | 1,075,000  |  |
| IPO (Net Proceeds)                | 25,400,000   | Options (WAEP \$0.74)            | 3,017,033  |  |
| S-3 Financings (Net Proceeds)     | 1,485,000    | Warrants (WAEP \$2.39)           | 761,741    |  |
| Total                             | \$31,425,000 | Total                            | 20,677,308 |  |

• Insider ownership (fully diluted): ~35%

## Value<br/>InflectionPotential Value Creating Milestones 2023-2025

Value-Generating Milestones with Potential to Create Multiple Liquidity Opportunities

external development

candidates



#### 2025

#### TTX-MC138

• Commercialize or commence Ph III

Advance next therapeutic candidate to clinic – Ph I

PNS