Platform of Targeted Therapeutics to Treat Metastatic Disease

Michael Dudley, Co-Founder, CEO
email: michael.dudley@transcodetherapeutics.com

Contents

Executive Summary

Therapeutic Solutions to Address 90% of Cancer Deaths

Problem: 90% of cancer deaths attributed to metastasis, not primary tumors from which they originate

Mission: Focus on treating Metastasis, Cancers that spread to other parts of the body

TransCode Discovery:

Metastatic tumor cells cannot survive without the overexpression of a specific non-coding RNA molecule, microRNA-10b, which regulates the viability of metastatic tumor cells.

microRNA-10b over-expression is validated in more than 18 different tumor types.

Inhibiting microRNA-10b → death of metastatic tumor cells → treating metastasis

TransCode has found a way to inactivate microRNA-10b resulting in the complete regression of established metastases with no recurrence and no toxicity.

TransCode has developed a portfolio of targeted therapeutics addressing multiple tumor types

TTX-MC138, TransCode's patented lead therapeutic, licensed from Massachusetts General Hospital, has achieved proof of concept both *in vitro* and *in vivo. In addition,* TransCode has also developed, patented and licensed a companion Biomarker test for non-invasive detection of microRNA activity.

Team

Board of Directors

- Michael Dudley, Co-Founder, CEO
- Thomas Fitzgerald, MBA, CFO
- Philippe Calais, PhD, Former CEO of Isarna Therapeutics B.V.

Management Team

- Michael Dudley, CEO
- Thomas Fitzgerald, MBA, CFO
- Oliver Steinbach, PhD, VP R&D*
- Zdravka Medarova, PhD, Co-Founder, Drug Discovery*
- Alan Freidman, Investor Relations

(* Identified individuals to be phased in once capitalized)

Corporate/Scientific Advisors

- Anna Moore, PhD, Co-Founder, Professor of Radiology and Physiology, Michigan State University
- Richard Peters, MD, PhD, President/CEO/Director, Merrimack Pharmaceuticals
- Jack Henneman, JD, Former CFO, NewLink Genetics
- Keith Flaherty, MD, Director of Termeer Center for Targeted Therapy, MGH Cancer Center
- Raghu Kalluri, MD, PhD, MD Anderson Cancer Center
- George Calin, MD, PhD, MD Anderson Cancer Center
- Carlo Croce, MD, Ohio State University Cancer Center
- Dmitry Samarsky, PhD, CTO, Sirnaomics
- Peter Ordentlich, PhD, CSO and Founder, Syndax
- Betsabeh Madani, MBA, MEng, EIR, Innovation Blvd.

Intellectual Property

Lead Therapeutic - *Therapeutic Nanoparticles and Methods of Use Thereof*

- Composition of Matter for TTX-MC138 (Patent expected to issue Q1 2019). Expires 2032
- Method Patent for treating metastatic breast cancer (Issued 4/17). Expires 2032

Biomarker - *miRNA Profiling Compositions and Methods of Use*

- Nanosensor for non-invasive detection of microRNA activity (Issued 10/2/18). Expires 2034

Freedom to Operate (FTO)

- FTO completed on IP for TTX-MC138 by Goodwin Law LLP

IP License

- Exclusive worldwide license with MGH signed November 22, 2018

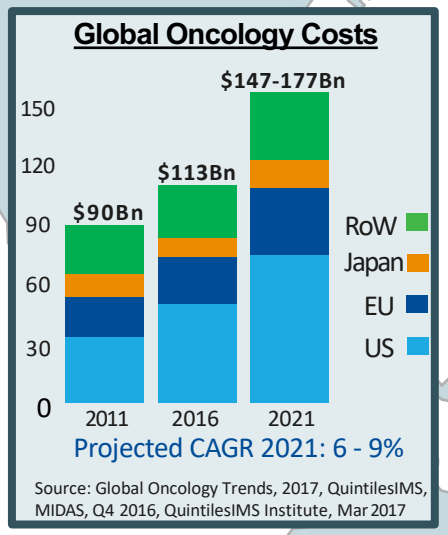
In 2018, cancer will be responsible for 9.6 million* deaths globally and 90% are attributed to metastasis

Global costs of Metastatic Cancer therapeutics exceed 50% of all Cancer costs with $54.11 billion in 2017 - anticipated to reach $98.24 billion by 2025.**

Metastasis Treatments:
Limited Options
Poor survival rates***

Annual Cancer Deaths*
Global: 9.6M in 2018
US: 0.61M in 2018

Cancer Deaths in 2018: *
Lung 1.76M
Colorectal 0.86M
Stomach 0.78M
Liver 0.78M
Breast 0.63M



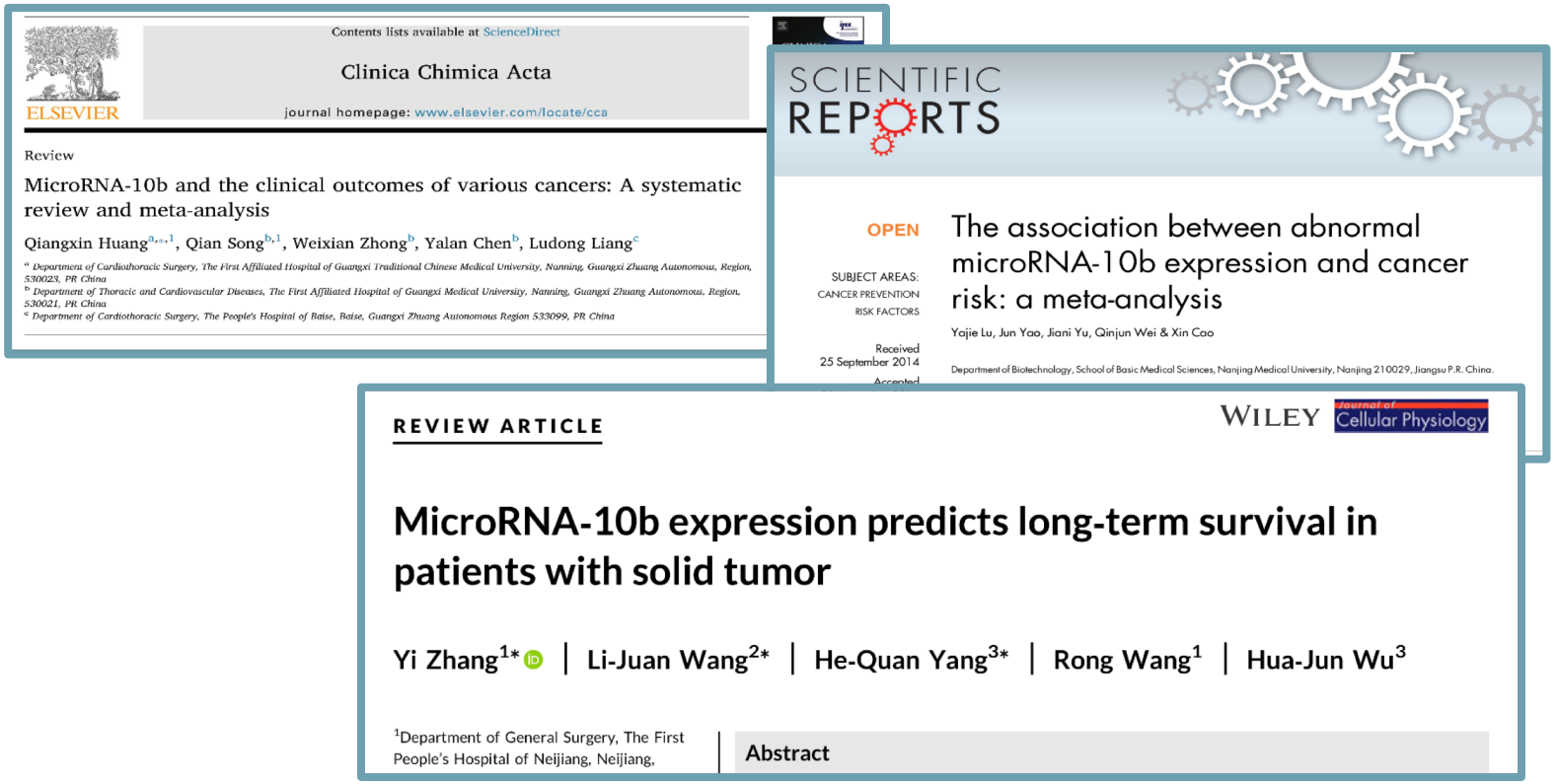
*** 72 cancer therapies approved from 2002-2014 led to 2.1 months average extended life expectancy

* World Health Organization: http://www.who.int/news-room/fact-sheets/detail/cancer
**IQVIA Institute for Human Data Science

Identifying a Metastasis Target

Association of microRNA-10b and metastasis (spread of cancer) is extensively validated*

Across 18 > tumor types, over 120 studies (including a number of meta analysis publications) on microRNA-10b and metastasis have been published



Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

ELSEVIER

Review

MicroRNA-10b and the clinical outcomes of various cancers: A systematic review and meta-analysis

Qiangxin Huang[a,*,1], Qian Song[b,1], Weixian Zhong[b], Yalan Chen[b], Ludong Liang[c]

[a] Department of Cardiothoracic Surgery, The First Affiliated Hospital of Guangxi Traditional Chinese Medical University, Nanning, Guangxi Zhuang Autonomous, Region, 530023, PR China
[b] Department of Thoracic and Cardiovascular Diseases, The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi Zhuang Autonomous, Region, 530021, PR China
[c] Department of Cardiothoracic Surgery, The People's Hospital of Baise, Baise, Guangxi Zhuang Autonomous Region 533099, PR China

SCIENTIFIC REPORTS

OPEN

SUBJECT AREAS:
CANCER PREVENTION
RISK FACTORS

Received
25 September 2014

The association between abnormal microRNA-10b expression and cancer risk: a meta-analysis

Yajie Lu, Jun Yao, Jiani Yu, Qinjun Wei & Xin Cao

Department of Biotechnology, School of Basic Medical Sciences, Nanjing Medical University, Nanjing 210029, Jiangsu P.R. China.

REVIEW ARTICLE

WILEY Journal of Cellular Physiology

MicroRNA-10b expression predicts long-term survival in patients with solid tumor

Yi Zhang[1*] | Li-Juan Wang[2*] | He-Quan Yang[3*] | Rong Wang[1] | Hua-Jun Wu[3]

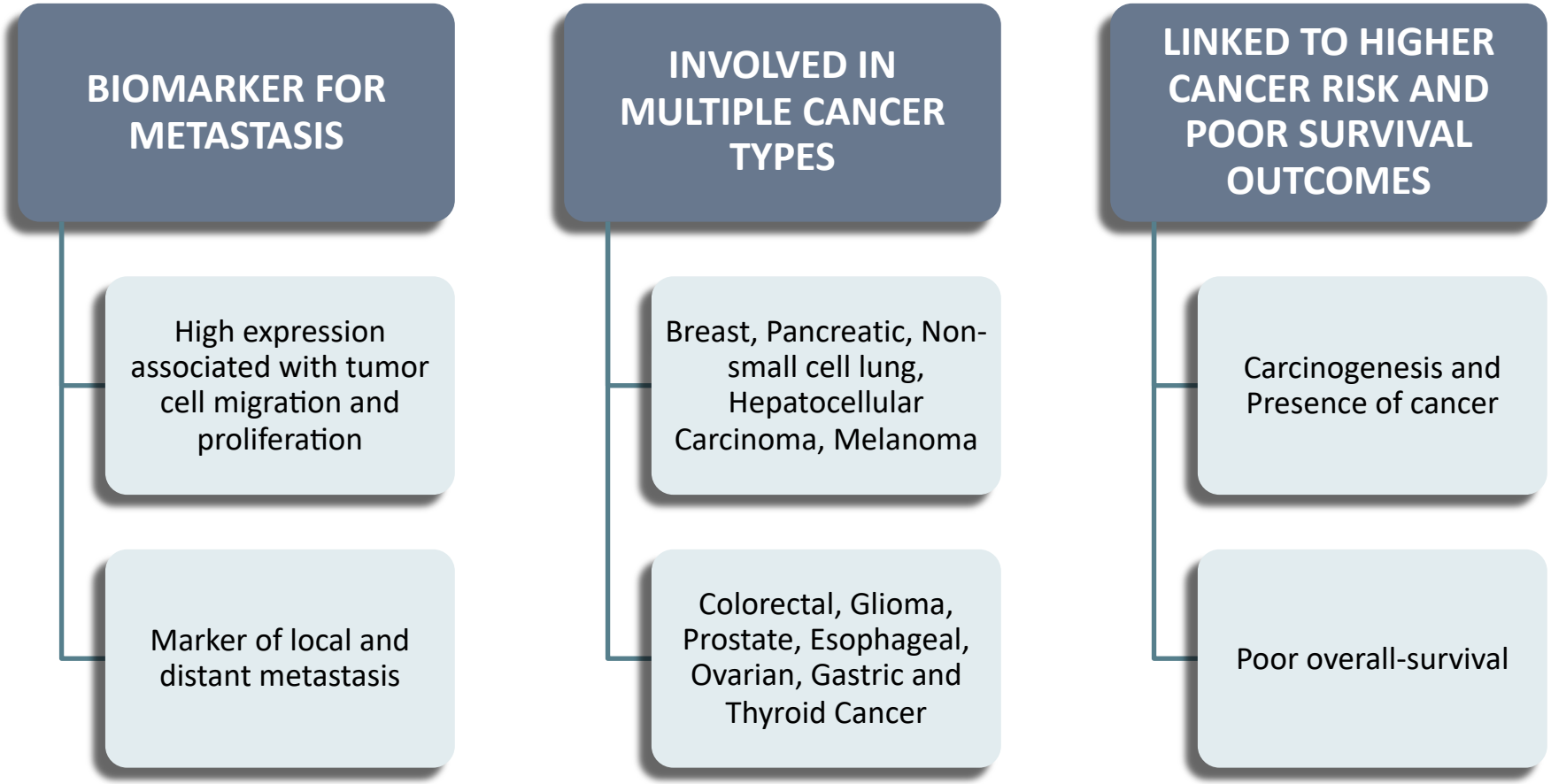
[1]Department of General Surgery, The First People's Hospital of Neijiang, Neijiang,

Abstract

* See Appendix slides for a list of scientific references

Why microRNA-10b? A Unique Biomarker

4 separate meta-analysis studies involving 7,237 patients showed microRNA-10b:

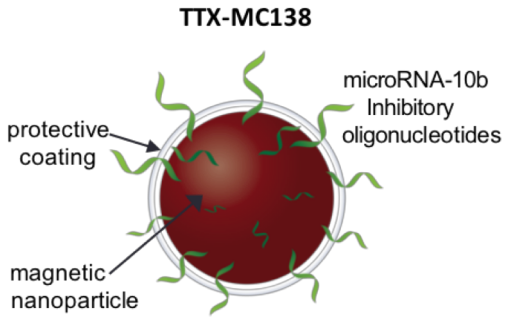


Solution: Proprietary Targeted Solution

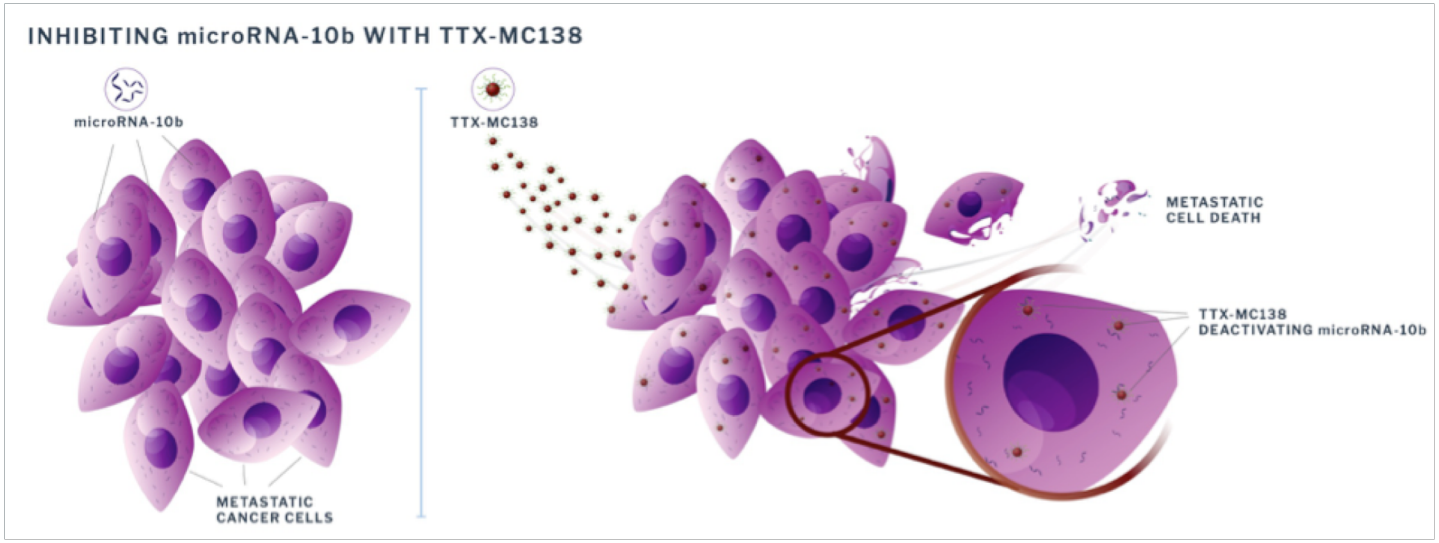
Lead Therapeutic Candidate: TTX-MC138

IONP + Inhibitory Oligonucleotide sequenced to miRNA-10b

- ✓ Eliminates metastasis by inhibiting microRNA-10b
- ✓ Inhibition results in death of metastatic tumor cells
- ✓ Proven delivery system optimized for designated target
- ✓ Image guided delivery key competitive advantage
- ✓ Unique capability to accumulate at metastatic sites



TTX-MC138: Mechanism of Action: Eliminates metastasis by inhibiting microRNA-10b



Delivery System Comparison

Company	Delivery system	Particle size	Zeta Potential* +0-60 scale	Toxicity potential Scale 0-10	Immunogenicity potential Scale 0-10	LNAs	Comments
TransCode Therapeutics	**Iron oxide nanoparticles (Image capable)**	**20 nm**	**+50 mV**	**0-2**	**0-2**	**Yes**	**Dextran coating = rapid uptake**
MiRNA	Lipid nanoparticles	120 nm	+20 mV	8-10	8-10	No	Patient deaths in clinic due to high toxicity
Miragen	Modified oligonucleotides	NA	-	0-2	0-2	Yes	Off target effects due to lack of a carrier for delivery
Regulus Therapeutics	GalNAc-conjugation; Lipid nanoparticles	100 nm	+20 mV	8-10	8-10	No	Cancelled clinical due to high toxicity
Arcturus Therapeutics	LUNAR® Lipid nanoparticle	40-50 nm	neutral	unknown	unknown	No	None
Santaris (Roche)	Modified oligonucleotides	NA	-	2-4 due to targeting the liver	2-4	Yes	Well tolerated in clinical trials

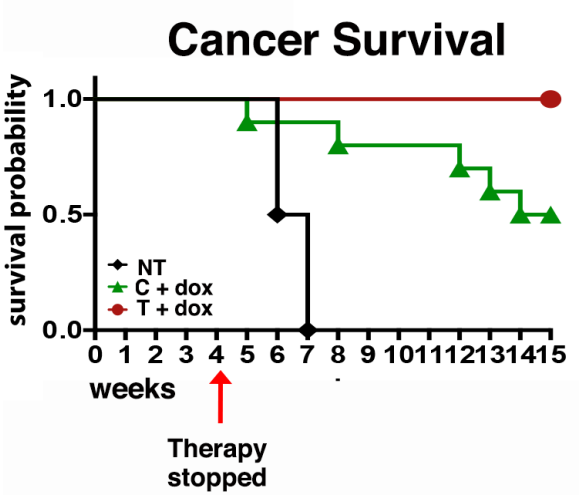
* Higher value associated with greater stability in solution

Proof of Concept

Pre-Clinical POC: TTX-MC138

Stage II/III Metastatic Triple-Negative Breast Cancer, Mouse Model

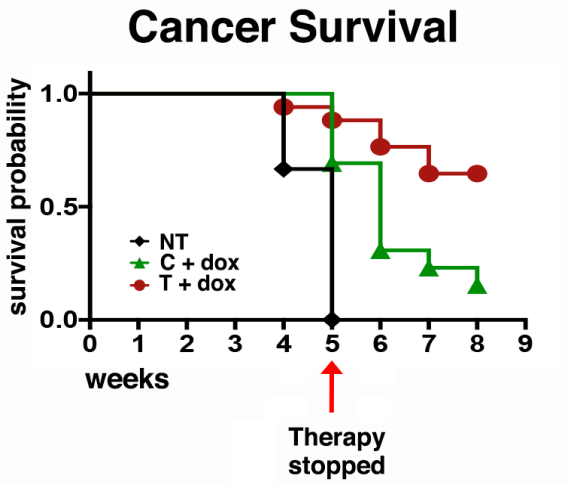
- TTX-MC138 superior to control + low-dose doxorubicin*
- Eliminates pre-existing ***local*** metastases



After metastases were eliminated, the therapy was stopped in both models and there was no recurrence or toxicity

Stage IV Metastatic Triple-Negative Breast Cancer, Mouse Model

- TTX-MC138 superior to control + low-dose doxorubicin*
- Eliminates pre-existing ***distant*** metastases

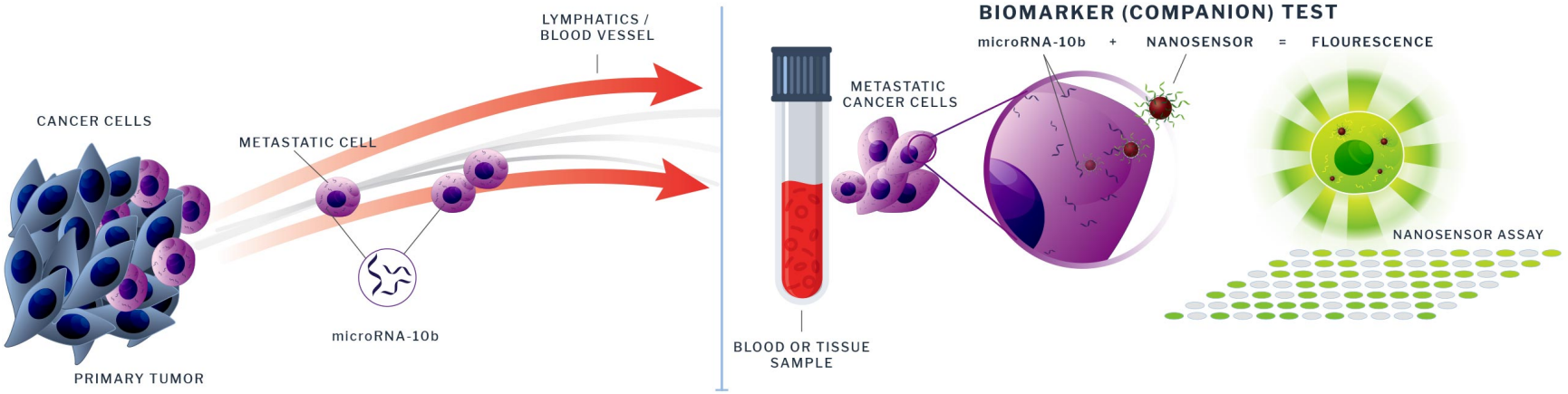


NT - No therapy
C - Control (Irrelevant oligo)
T - TTX-MC138
dox - low-dose doxorubicin

**Doxorubicin was used to slow down cell division in tumor cells. In pre-clinical studies that utilize aggressive metastatic tumor models, the use of doxorubicin was necessary to allow TTX-MC138 to fully inhibit microRNA-10b. Because metastatic growth is slower in humans, the use of a cytostatic such as doxorubicin will likely be unnecessary, and TTX-MC138 would be administered as a monotherapy.*

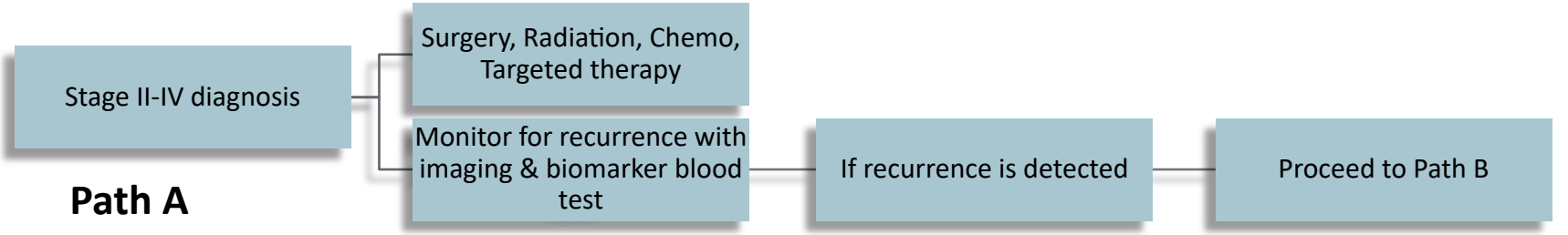
Biomarker Test

- TransCode's predictive biomarker nanosensor has the unique capability of microRNA profiling in intact live cells and tissues.
- The fluorescent read-out generated by the nanosensor is highly specific and has nanomolar sensitivity.



Biomarker Test Utility

Early detection reduces mortality in Cancer patients. Expression of microRNA-10b can be used as a diagnostic biomarker to detect the presence of metastasis as well as a biomarker to predict overall survival and disease-free survival in cancer. TransCode has patented a biomarker test to measure the expression of any microRNA in patients.



Path A

Path B

Therapeutic Pipeline*

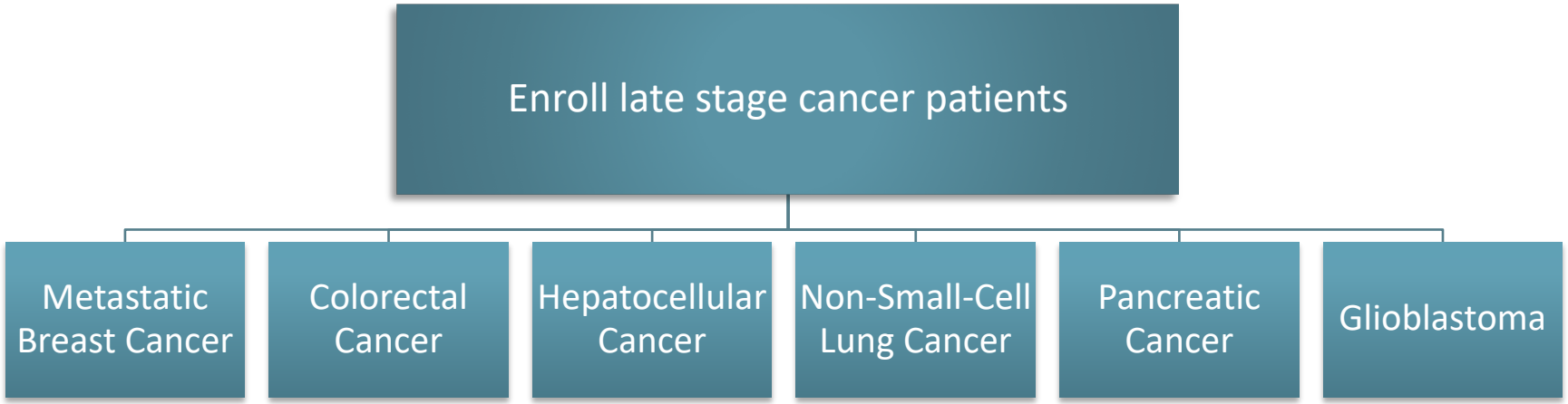
Therapeutic	Target	Discovery	*In vitro***	Preclinical	Phase II/III
TTX-MC138	miR-10b	MTNBC			
	miR-10b	Colorectal cancer			
	miR-10b	NSCL cancer			
	miR-10b	Pancreatic cancer***			
	miR-10b	Glioblastoma**			
	miR-10b	Hepatocellular cancer***			
Lin28b Inhibitor	Lin28b	Pancreatic cancer***			
anti-miR-xxx	miR-xxx	Other cancer types			
siRNA	PD-L1	Pancreatic Cancer***			

*Pipeline currently in development – selected therapeutics and targets may change

** TTX-MC138 demonstrated therapeutic efficacy *in vitro* in 77% of 624 human tumor cell lines representing the spectrum of metastatic and non-metastatic cancers. *PLOS ONE | https://doi.org/10.1371/journal.pone.0201046 July 2018*

***Cancer types classified as orphan diseases

Clinical POC Strategy: Adaptive Trial Design



- PhIIa trial - Single IND
- Up to 6 different tumor types
- Patients with cancer types with known microRNA-10b over-expression
- Enroll additional patients in the arm showing the greatest success
- Enable continuation from PhIIa – to PhIII

Therapeutic Programs – Projected Milestones

(Subject to Pre-IND meeting with FDA)

Program		Timeline			
Therapeutic	Cancer Type	2019	2020	2021	2022
TTX-MC138	MTNBC				
	Colorectal				
	NSCL				
	Pancreatic				
	Glioblastoma				
	Hepatocellular				
Lin28b Inhibitor*	Pancreatic				
siRNA*	Pancreatic				

* License in process

Funding

Investment to date

- **$550,000**
  - MGH License
  - New Website
  - Patent Expenses
  - Marketing Communications
  - Other Legal expenses
- **Grants to date $5.3M***
  - Therapeutic development
  - Biomarker development
  - Preclinical POC

*NIH Grants to researchers while at MGH

Seed Round

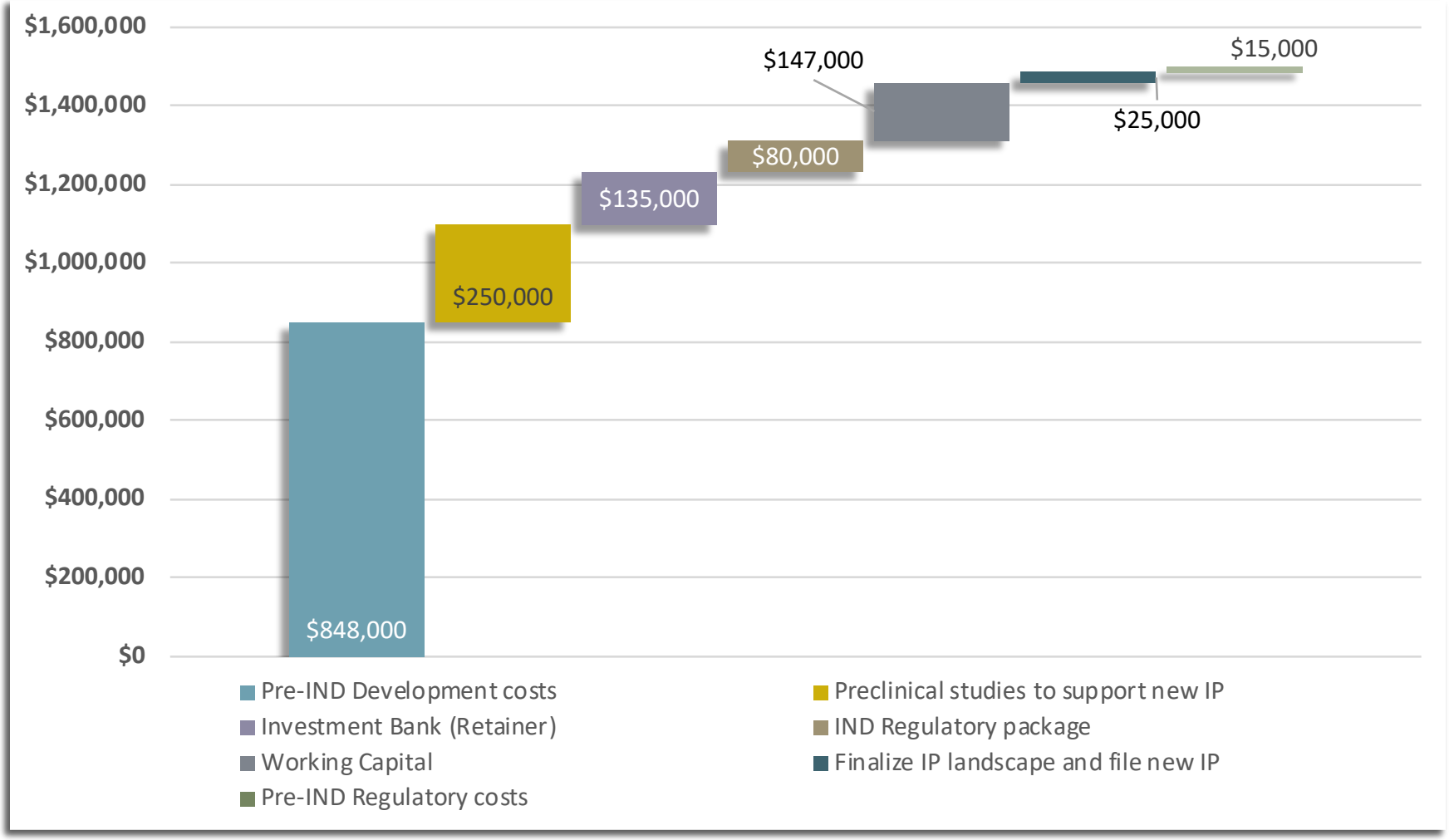
- **Up to $1.5M Convertible note**
- **Converts to Series A valuation**
  - Pre-IND development costs
  - Develop and file new intellectual property
  - Conduct preclinical studies supporting new IP
  - Retain Investment Bank
  - Pre-IND meeting with FDA
  - IND Regulatory package

Series A Investment Round

- **Investment Bank - Outcome Capital****
- **$36M Series A Preferred**
  - Hire management team
  - IND Enabling Studies - TTX-MC138
  - File IND
  - Phase IIa clinical trial
  - Achieve clinical POC
  - Expand IP portfolio
  - In-license other microRNA assets

** www.outcomecapital.com

Seed Round Use of Proceeds



Path to Liquidity