# THiogenesiS THerapeuticS

## Corporate Overview

Sept - 2025

(TSXV: TTI / OTCQX: TTIPF)

# Forward Looking Statement

This document and any attachments are intended for information purposes only and should not be construed as on offer or solicitation for the sale of securities. Statements in this presentation include forward-looking statements within the meaning of certain securities laws. These forward-looking statements include, among others, statements with respect to our objectives, goals and strategies to achieve those objectives and goals, as well as statements with respect to our beliefs, plans, objectives, expectations, anticipations, estimates and intentions. The words "expected to" "illustrate" "has the potential to" "will be", "evaluating" "plans" "can be" "planning" "to predict" "potential" "may" "should" and words and expressions of similar import, are intended to identify forward-looking statements.

Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not put undue reliance on these statement or the scientific data presented as a number of important factors, many of which are beyond our control, could cause our actual results to differ materially from the beliefs, plans, objectives, expectations, anticipations, estimates and intentions expressed in such forward-looking statements. We do not undertake to update any forward-looking statements, whether written or oral, that may be made from time to time by us or on our behalf; such statements speak only as of the date made. The forward-looking statements included herein are expressly qualified in their entirety by this cautionary language.

# Thiogenesis Therapeutics

## Investment Highlights

***TTI-0102 unlocks the potential of cysteamine by eliminating its historical limitations***

- ***Cysteamine has demonstrated therapeutic potential beyond cystinosis*** (e.g. mitochondrial disease, pediatric MASH and Huntington's disease) but has been hindered by GI side effects and dosing challenges (*Procysbi*®)
- **TTI-0102** ***improves bioavailability and tolerability*** via a novel sulfur-based prodrug design, allowing for higher dosing with fewer side effects, as confirmed in Phase 1 trials
- ***Now advancing in a Phase 2 EU trial for MELAS***, a rare mitochondrial disease with no approved therapy, TTI-0102 replenishes glutathione and taurine, both deficient in MELAS patients
- ***Compelling valuation with significant upside relative to rare disease peers,*** with optionality across its broader pipeline – Leigh's and pediatric MASH – targeting redox and metabolic dysfunction

# Experienced Leadership

## Christopher M. Starr, PhD

*Chairman of the Board*

- Co-Founder & Executive Chairman, **Monopar Therapeutics** (Nasdaq: MNPR)
- *Co-founder & CEO, **Raptor Pharmaceutical** (Nasdaq: RPTP)*
  *- Acquired by Horizon Therapeutics for **$800M** in 2016*
- Co-Founder & SVP/CSO, **BioMarin Pharmaceutical** (Nasdaq: BMRN)
  - Led development and FDA approvals of **Aldurazyme**, **Naglazyme** and **Kuvan**

## Patrice Rioux, MD, PhD

*Founder, CEO, Director*

- *CMO & Head of Regulatory Affairs, Raptor Pharmaceutical*
  *- Led **FDA approval for Procysbi®,** a delayed-release cysteamine therapy*
- CMO, **Edison Pharmaceuticals**
- Senior roles at **Repligen** (Nasdaq: RGEN), **Biogen** (Nasdaq: BIIB) and **Variagenics**

# Thiogenesis - Summary

**Thiogenesis Therapeutics (TSXV: TTI) is a clinical-stage biotech company, developing therapeutic compounds to treat pediatric diseases with unmet needs**

- ***Cysteamine-based thiol drugs (R-SH)*** *have demonstrated efficacy in multiple indications, but dose-limiting side effects have hindered their commercial use*
- Lead compound, *TTI-0102*, is an asymmetric disulfide that provides a controlled release of cysteamine
- *Phase 1 human data has already demonstrated that TTI-0102 is well-tolerated at high doses – up to 4 times the equivalent of generic cysteamine (Cystagon®)*
- *TTI-0102* has the *potential to be best-in-class compound for generating intracellular cysteine,* a critical amino acid that is a precursor to 2 important compounds that combat oxidative stress: **glutathione and taurine**
- *Cost and time efficient strategy for rapid clinical validation:*
  - ◊ 505 (b)(2) regulatory pathway (prodrug strategy)
  - ◊ Small, targeted human trials
  - ◊ Targeting large, unmet medical markets

# TTI-0102 Lead Indications

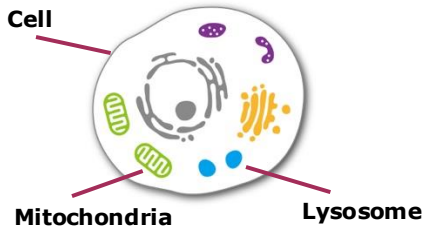
| Mitochondrial Diseases (orphan)<br>N = 75,000 (US)*<br>Multi-billion TAM<br>* MELAS and LS are approx. 15,000 (20%) of mito diseases | | Pediatric MASH<br>N > 1,500,000 (US)<br>Multi-billion TAM |
|---|---|---|
| MELAS | Leigh Syndrome (LS) | Pediatric MASH |
| **Phase 2** | **Phase 2a** | **Phase 2**<br>(Filing IMPD) |
| Double Blind | Double Blind | - |
| EU | US | EU |

# Cysteamine - Untapped Potential

- Thiols like cysteamine have a functional –*SH* group (sulfur & hydrogen) that is active in biochemical reactions, *a sulfur containing compound,* it has been limited by its GI side effects and dosing limitations

- Cysteamine-based drugs have only been approved for cystinosis which affects ~ 1,000 patients in the U.S.
  *Raptor - Delayed Release Cysteamine (Procysbi® - 2013)*

- ***Procysbi® Progressed Into Trials in Bigger Indications***
  - *Huntington's disease (France) 40,000 patients*
  - *Mitochondrial diseases (Stanford) 75,000 patients*
  - *Pediatric NAFLD/NASH (NIH) >1,500,000 patients*




- *All three showed promise but did not advance,* ***because side effects limited dosing necessary to restore mitochondrial dysfunction***

raptor pharmaceutical corp.

PROCYSBI (cysteamine bitartrate) delayed-release capsules delayed-release oral granules

# Inherited Mito Disease Trial with *RP103*

- Open-label evaluation of the safety/tolerability, PK/PD, and efficacy of RP103 (*Procysbi® or* delayed release cysteamine) in patients with inherited mitochondrial disease

- N=36 patients were enrolled across a broad group of inherited mitochondrial diseases; ***including MELAS (6), Leigh syndrome (9),*** Leber's, MERFF, POLG, etc.

- *RP103 did not meet its efficacy endpoint, which was based on the Newcastle Pediatric Mitochondrial Disease Scale (NPMDS), which* has limitations measuring treatment effects in short-term clinical trials, *as compared to a 12-minute walk test*

- RP103 was safe and there was evidence of patient improvement based on ***feedback and patients voluntarily entering an extension study with RP103; some have enquired about entering TTI-0102 clinical trials***

- **Increased GSH was observed** in patients over 24 weeks, but the oxidized glutathione (GSSG) remained stable, improving the GSH:GSSG ratio is an indicator of improvement in oxidative stress
  (Enns, et al. 2014)

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PROCYSBI® (cysteamine bitartrate) delayed-release capsules delayed-release oral granules

# Pediatric MAFLD Trial with *RP103*

## CyNCh Trial (NIH)

- NIH sponsored trial, ***N=169 children with MAFLD were treated with low dose of Procysbi,*** the children ranged from 50-90 kgs
- Did not meet the primary endpoint for the overall group, of histologic improvement
- *(2012–2015 - ClinicalTrials.gov Identifier: NCT01529268)*

## CyNCh - *Secondary Analysis*

- Post-hoc analyses, the smaller children (≤65 kgs) **did have a 4-fold better chance of histologic improvement (P=.005)**
- Dosing was uniformly low – better results in smaller children most likely due to receiving a higher ratio of drug per kg of body weight
- Overall improvement in biomarkers

Schwimmer J. *et al.*, 2016, Gastroenterology

# TTI-0102 ➡ Metabolized into Cysteamine

**TTI–0102**
**(Composition)**

- Disulfide consisting of 2 thiols
- Cysteamine and Pantetheine
- Oral administration

**Transformation One**

- First in the GI tract, TTI-0102 is reduced into 2 separate thiols -
  - ➢ Cysteamine #1
  - ➢ Pantetheine

**Transformation Two**

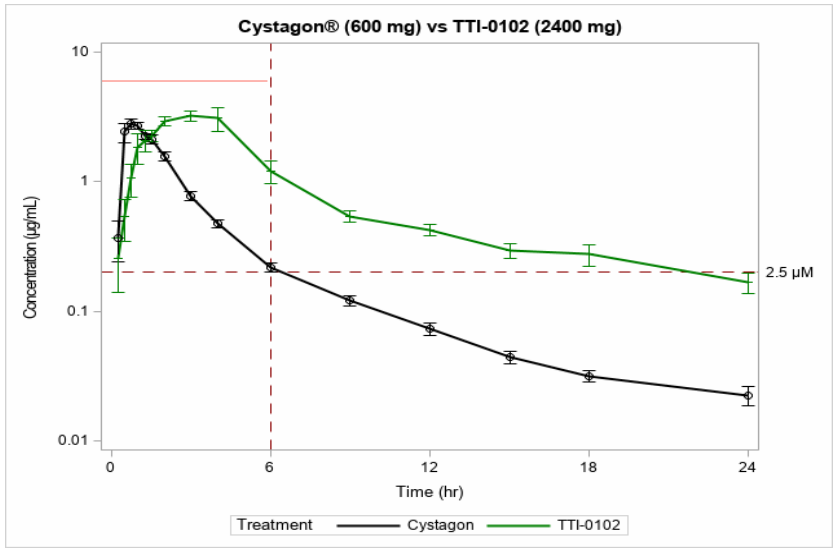
- Then in the colon or small intestine pantetheine is hydrolyzed into -
  - ➢ Cysteamine #2
  - ➢ Pantothenic acid ($B_5$)

Both transformations occur in a controlled manner, acting as a 'gating metabolic mechanism' and **eliminating the spike** in cysteamine that is associated with side effects

# TTI-0102 Lead Compound

- *TTI-0102* is a proprietary, engineered disulfide that is a precursor to cysteamine
- A unique **'gating metabolic mechanism'** enables sustained intracellular release of cysteamine, allowing for potential once-daily dosing

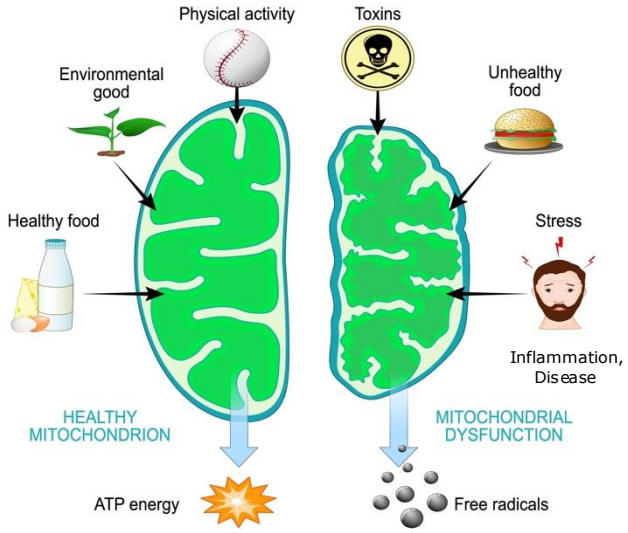
## Phase 1 Study (PK/Safety)




- ***TTI-0102* was dosed at 4x** the therapeutic level of Cystagon® (generic cysteamine) in healthy volunteers; it was well-tolerated with no side effects and has potential for once-a-day dosing

# Mitochondrial Dysfunction and Oxidative Stress

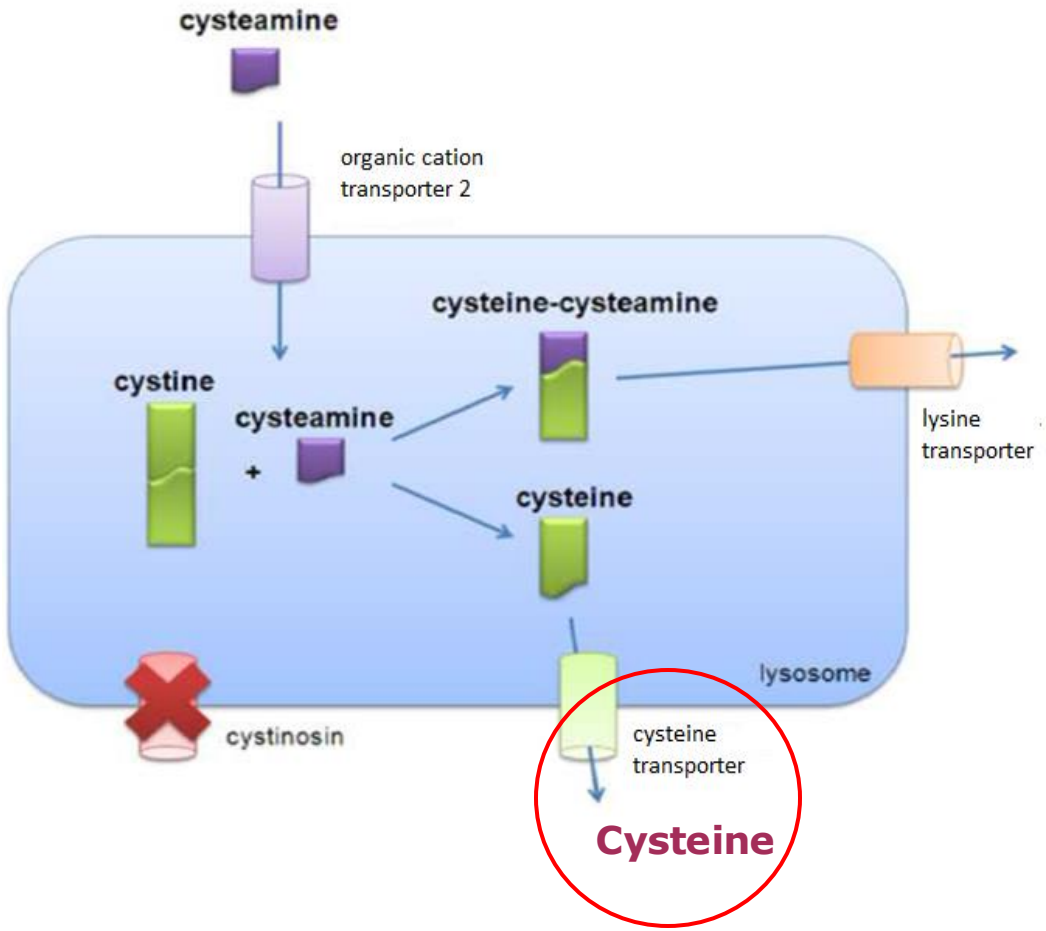
*Mitochondria generate the energy required to power cells*




- ***Unhealthy mitochondria produce too many reactive oxygen species (ROS) or free radicals***, unstable molecules that damage DNA, proteins, and membranes - leading to oxidative stress and mitochondrial dysfunction - central to many diseases

- ***Glutathione (GSH) is the body's master antioxidant*** and is uniquely transported into the mitochondria. Boosting GSH levels helps neutralize excess ROS, restore mitochondrial balance, and improve cell function

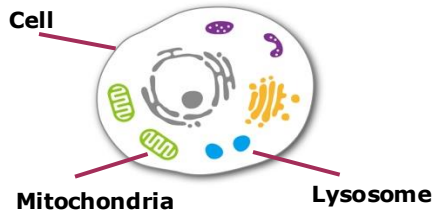
# Cysteamine ➞ Cystine Depletion ➞ GSH




*Besouw M - Adapted from et al. Drug Discovery Today, 2013*

## Production of Intracellular GSH

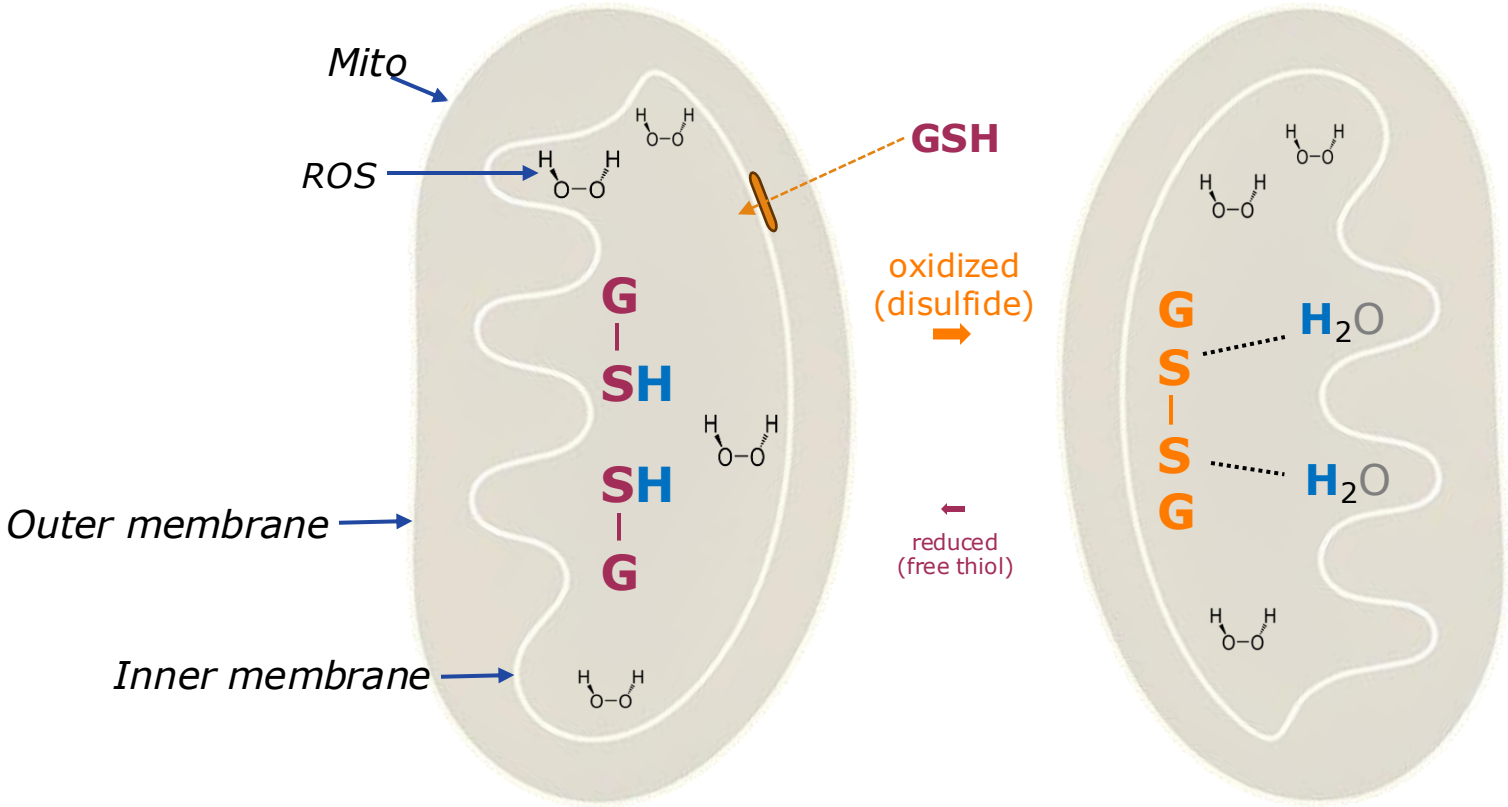
- Cysteamine breaks down cystine – *highly concentrated in the lysosome* - into 2 unique thiols that can exit into the cytoplasm
- Increases free intracellular cysteine, which *is the limiting factor in glutathione (GSH) synthesis*
- *Glutamic Acid* + ***Cysteine*** + *Glycine* = ***GSH***
- GSH is considered the "master" antioxidant, and uniquely enters the mitochondria through a dedicated transporter



# Thiol/Disulfide - Antioxidation

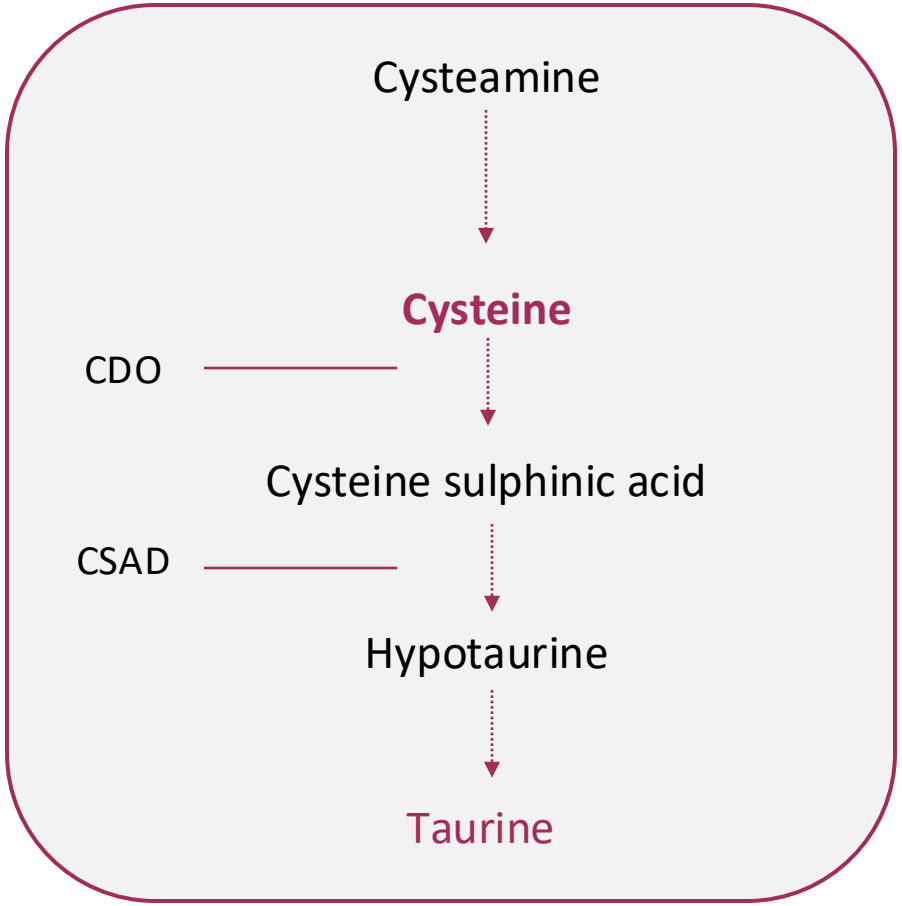
***TTI-0102 → Cysteamine → Cysteine → Glutathione (GSH)***

*TTI-0102 is a platform technology with a core functionality of restoring mitochondrial health*



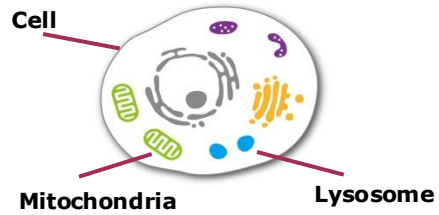

- *GSH oxidizes into GSSG – releasing hydrogen that transforms the ROS into harmless water molecules*
- ***It is critical to supply enough GSH** to neutralize the abundant ROS to restore healthy mitochondrial function*

# TTI-0102 → Taurine

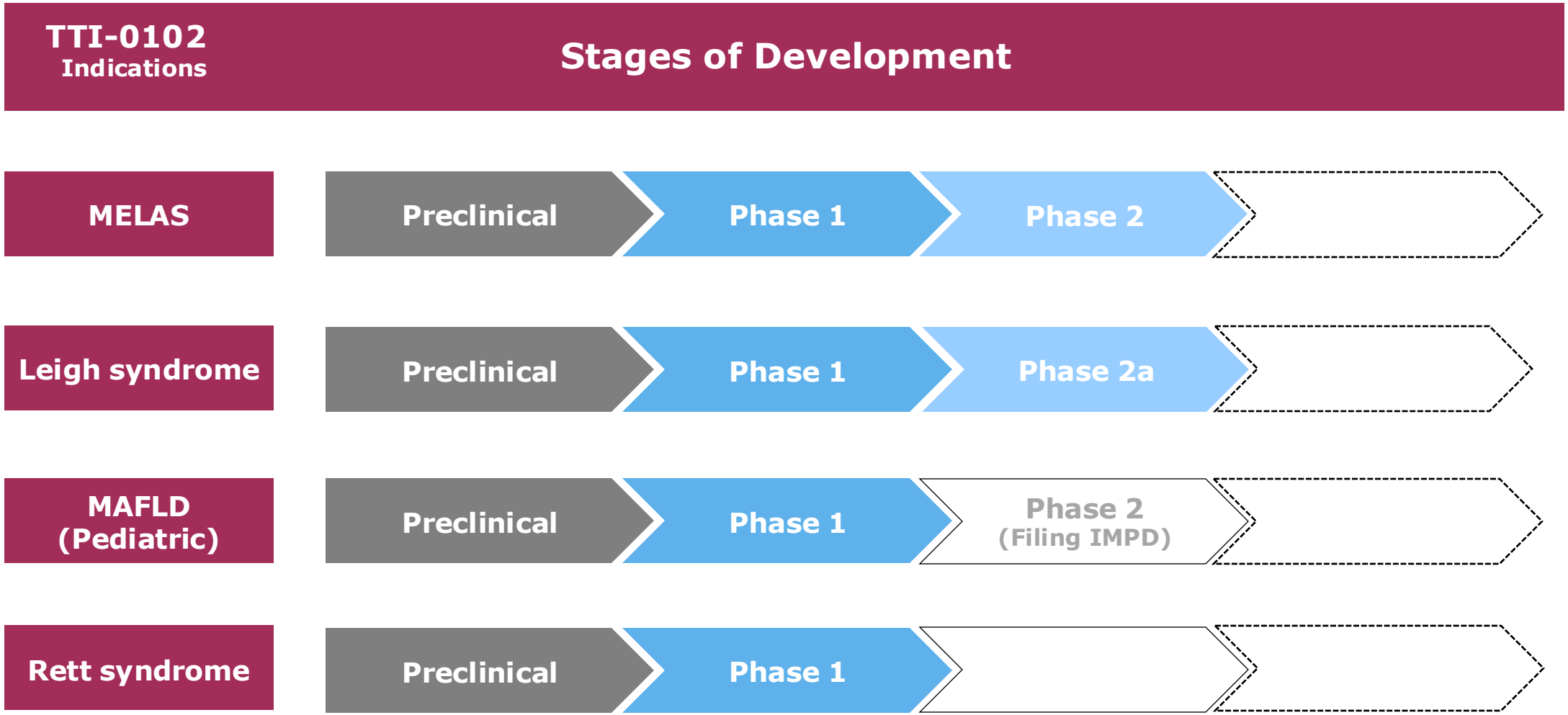



## Production of Intracellular Taurine

- In the lysosome, cysteamine reacts with cystine in a thiol-disulfide exchange, creating 2 unique thiols that can exit the lysosome, a disulfide and a free cysteine
- To synthesize taurine, the intracellular free cysteine *goes through two enzymatic reactions to create hypotaurine*
- *Hypotaurine is then oxidized into the amino acid taurine*
- ***Taurine combats oxidative stress and helps maintain mitochondrial function***



# Thiogenesis Pipeline



# MELAS

***Mitochondrial Encephalomyopathy, Lactic Acidosis & Stroke Like Episodes (MELAS)***

- **MELAS** is a rare, inherited mitochondrial disease caused by genetic mutations (**most often m.3243A>G in the MT-TL1 gene**); for which there are **no approved drugs in the EU or US**
- One of the more prevalent of the mitochondrial diseases - estimated to be **4.1 in 100,000**
- Symptoms include **fatigue/weakness, loss of motor skills, loss of appetite, seizures** and **stroke-like episodes**
- **MELAS patients exhibit oxidative stress**, and are typically **deficient in glutathione and taurine**
- ***TTI-0102*** *has potential as a therapy for MELAS because it increases the antioxidant glutathione and the amino acid taurine*
- There are **no approved drugs for MELAS** in the U.S. or EU
- Taurine has also been approved for the treatment of MELAS in **Japan** *(Ohsawa et al. 2019) – it has the potential to reduce seizures*
- Initiated **Phase 2 clinical trial in France/Netherlands in May 2025**

# MELAS – Phase 2 Trial (EU)

*'A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety, Tolerability, Efficacy, PK and PD of Oral **TTI-0102** for Treatment of Patients with MELAS'*

- **N=12 patients** will be enrolled in total, with **8 receiving TTI-0102** and **4 receiving a placebo** (**4 weeks of screening** + **24 weeks of treatment** = **28 weeks** total)
- **Primary efficacy endpoint**: **12 min walk test, secondary endpoints**: significant biomarkers
- *Interim assessment will occur after 6 patients have been treated for 3 months and 6 months, looking at safety/tolerability and efficacy*
- **Key Advisor**, Dr. Gregory Enns, Stanford
- Clinical sites in Europe:

  Dr. **Magalie Barth**, France
  Dr. **Mirian Janssen**, Netherlands

# Leigh Syndrome Spectrum ("LSS")

- **LSS is one of the most debilitating genetic diseases of the mitochondria** and shows up in infancy; it is **highly heterogeneous** involving mutations in both mitochondrial DNA and nuclear DNA
- Symptoms include **impaired sucking/breastfeeding**, **loss of mental and movement abilities**, **seizures**, **respiratory issues** and **poor muscle development**
- **Oxidative stress** and the damage caused by **mitochondrial dysfunction** are key features of LSS
- ***TTI-0102*** *has therapeutic potential by increasing glutathione and taurine*
- Estimated 1/40,000 live births
- **Thiogenesis received IND clearance on June 11, 2025**, to initiate a Phase 2a clinical trial
- **Announced collaboration with leading children's hospital** in the US to act as Lead Investigator

# LSS – Phase 2a Trial (U.S.)

*'A Double-Blind, Phase 2a trial to Evaluate the Efficacy and Safety of TTI-0102 in Leigh Syndrome'*

***Stage 1:***

- **A randomized, double-blind, placebo-controlled trial** enrolling 9 patients, with 6 receiving *TTI-0102* and 3 receiving placebo,
- This stage will **evaluate safety**, **tolerability**, **efficacy**, and **pharmacokinetics** / **pharmacodynamics** ("**PK/PD**") over a 3-month period, in adult and adolescent patients.

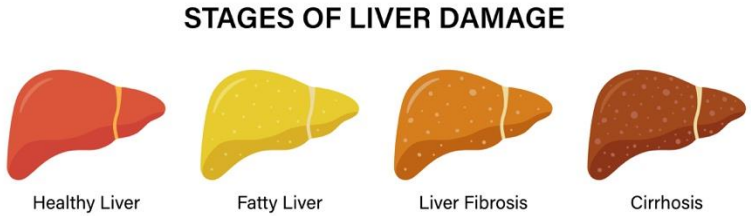
**Stage 2:**

- **An open-label extension of the trial**, enrolling 6 pediatric patients, 5 years and older, all being treated with *TTI-0102* for 3 months, to further assess safety, tolerability, efficacy, and PK/PD endpoints.
- **Key Advisor**, Dr. Gregory Enns, Stanford
- **Clinical site in U.S**. - Children's Hospital of Philadelphia ("CHOP"):

  Dr. Marni Falk
  Dr. Zarazuela Zolkipli-Cunningham

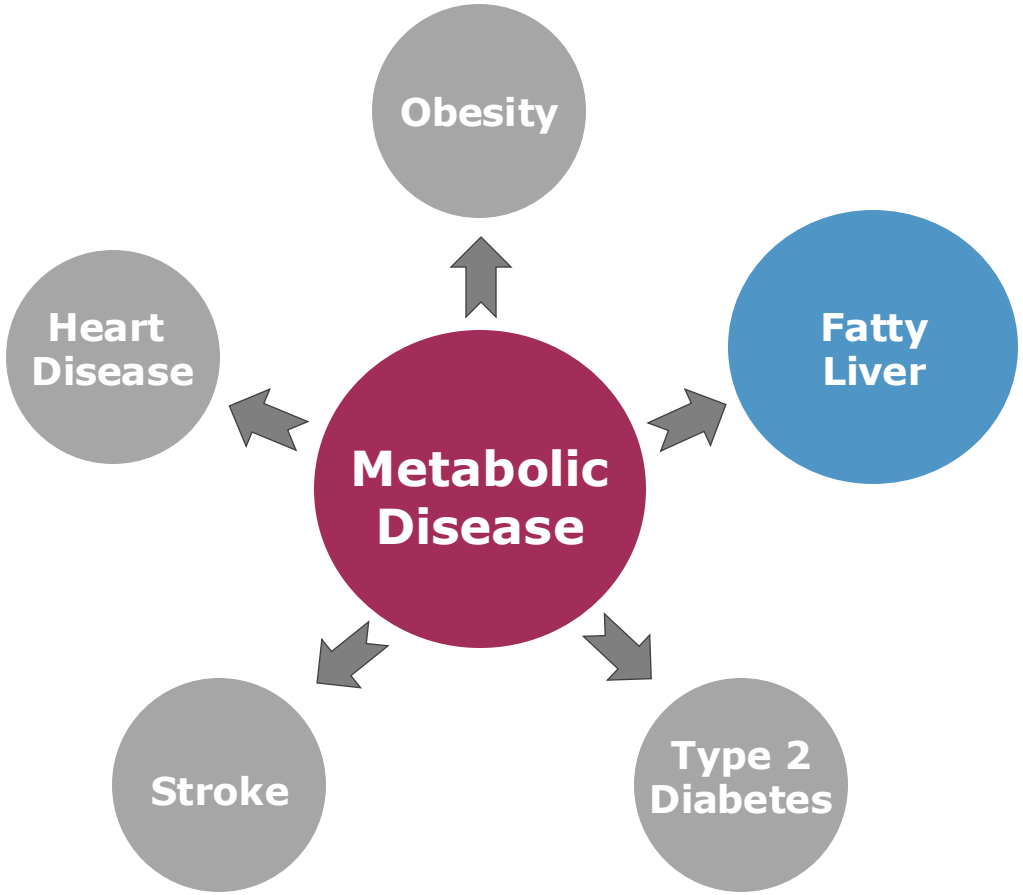
# Pediatric MASH

- ***Pediatric Metabolic Dysfunction-Associated Steatohepatitis (MASH)*** is an advanced disease of the liver in children; often linked to obesity and characterized by inflammation, accumulation of fat and scarring (fibrosis)




- **Prevalent and accelerating in children**, estimated to affect over **1.5 million in the US**
- Interventions, like *TTI-0102*, targeting oxidative stress in the mitochondria, have emerged as important therapeutic targets for MASH
- TTI-0102 also inhibits hepatic stellate cells ("HSC") by reducing cystine, HSC cells are an important contributor in building fibrosis in the liver
- **Pantothenic acid ($B_5$)** is critical in synthesizing fatty acids, which also contribute to fibrosis
- **Submission of an IMPD** to enter a **Phase 2 clinical trial** planned in 2025

# Oxidative Stress → Metabolic Syndrome




- Mitochondrial dysfunction and oxidative stress are critical features of diseases across metabolic syndrome
- Antioxidant replacement therapies have the potential to restore mitochondrial function
- Glutathione is the 'master' antioxidant because it is uniquely transported into the mitochondria and plays an important role in neutralizing free radicals and reducing inflammation
- TTI-0102 has the potential to be the best-in-class drug for the generation of intracellular glutathione and taurine
- *Potential to be complimentary to GLP-1 drugs*

# Scientific Advisory Board

## Dr. David Housman

- MIT, award winning professor of biology, known for his contribution to the study of Huntington's disease and as a co-founder of 5 biotech companies

## Dr. Gregory Enns

- Stanford University, professor of Medical Genetics and Director of Biochemical Genetics Program; focus on mitochondrial and lysosomal disorders

## Dr. Miriam Vos

- Emory University, professor of Pediatrics and Division of Gastroenterology, Hepatology and Nutrition, and Director of Pediatric Fatty Liver Program at Children's Healthcare of Atlanta

# Thiogenesis – Upcoming Milestones

**Potential milestones (6-12 months):**

| | | |
|---|---|---|
| *MELAS* | → | Initiated Phase 2 trial, Q3/2025 interim analysis |
| Leigh syndrome | → | Initiate Phase 2 trial Q1/2026 |
| Pediatric *MASH* | → | Filing IMPD - Phase 2 trial 2025 |
| *Rett syndrome* | → | Filing IMPD Phase 2/3 trial 2026 |

# Company Info

| | |
|---|---|
| **Thiogenesis Therapeutics** | (TSXV: TTI / OTCQX: TTIPF) |
| **Shares Issued** | 51.8m million |
| **Shares Fully Diluted** | 55.8 million |
| **Insiders (36%)** | 16.7 million |
| **Share Price (09/02/2025)** | $0.76 |
| **52 week high/low** | $0.80/C$0.51 |
| **Market Cap.** | $39.4 million |
| **Cash (06/30/2025)** | $1.8 million* |
| **Contact** | info@thiogenesis.com |

- Currency in Canadian dollars
- C$4.15 million non-brokered private placement closed July 30, 2025