

A red bracket graphic consisting of two horizontal lines with short vertical lines at each end, framing the company name.

THiogenesis THerapeuticS

Corporate Overview

July - 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 an 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

- Experienced leadership team in orphan drug development, including achieving regulatory approval with cysteamine (delayed-release)
- Lead compound, TTI-0102, is a 3rd generation version of cysteamine (controlled-release)
- Strong human evidence of efficacy shown by the active moiety in targeted indications, previously constrained by dosing limitations due to GI side effects
- Early clinical data in a healthy volunteer study has demonstrated that TTI-0102 is well tolerated at high doses
- Regulatory visibility in three strategic Phase 2 indications, including collaboration & consultation with prominent medical professionals and institutions in the field
- Near term human efficacy data in a multi-billion dollar addressable market with no approved drugs

Experienced Leadership

Christopher M. Starr, PhD – Chairman of the Board

- Co-Founder, Executive Chairman, Monopar Therapeutics (Nasdaq: MNPR)
- *Co-founder & CEO, Raptor Pharmaceutical (formerly Nasdaq: RPTP), Raptor was acquired by Horizon Therapeutics for \$800M in 2016*
- Co-Founder & SVP/CSO, BioMarin Pharmaceutical (Nasdaq: BMRN), gained marketing approval of Aldurazyme, Naglazyme and Kuvan

Patrice Rioux, MD, PhD – Founder, CEO, Director

- *CMO and Head of Regulatory Affairs, Raptor Pharmaceutical, gained marketing approval for PROCYSBI® - delayed release cysteamine*
- CMO, Edison Pharmaceuticals
- Senior roles at Repligen (Nasdaq: RGEN), Biogen (Nasdaq: BIIB) and Variagenics



BiOMARIN



RepliGen



Thiogenesis - Summary

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

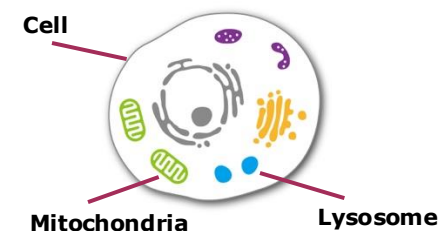
- *Cysteamine-based drugs are thiol compounds (R-SH) that have been well-studied and demonstrated efficacy in multiple indications, but dose-limiting side effects have limited their commercial development*
- Lead compound, TTI-0102, is an asymmetric disulfide that provides a controlled release of cysteamine
- *Phase 1 human data has already demonstrated that TTI-0102 is well-tolerated at high doses – up to 4x the generic version (Cystagon®)*
- *TTI-0102 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 model to achieve significant human efficacy data:*
 - ♦ Prodrug, 505 (b)(2) regulatory pathway
 - ♦ Small, confirmatory human trials
 - ♦ Unmet medical needs in large markets

TTI-0102 Lead Indications

Mitochondrial Diseases (orphan) N = 75,000 (US)* Multi-billion TAM <small>* MELAS and LS are approx. 15,000 (20%) of mito diseases</small>		Pediatric MASH N > 1,500,000 (US) Multi-billion TAM
MELAS	Leigh Syndrome (LS)	Pediatric MASH
Phase 2	Phase 2a	Phase 2 (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, *but as a sulfur containing drug*, it has been limited commercially by its GI side effects & short half-life
- Cysteamine-based drugs have only been approved for cystinosis and has 1,000 patients in the US - *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**



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)



Pediatric NAFLD Trial with *RP103*

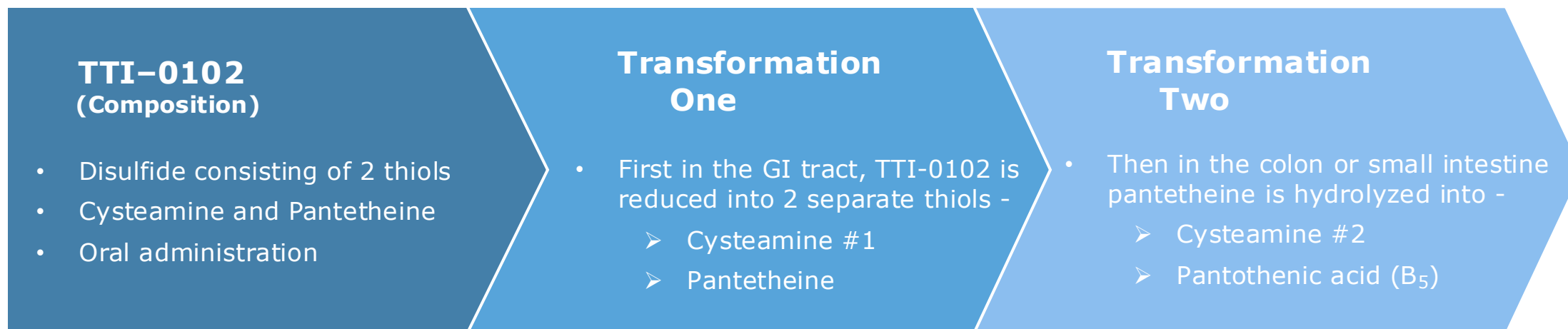
CyNCh Trial (NIH)

- NIH sponsored trial, ***N=169 children with NAFLD 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

TTI-0102 → Metabolized into Cysteamine

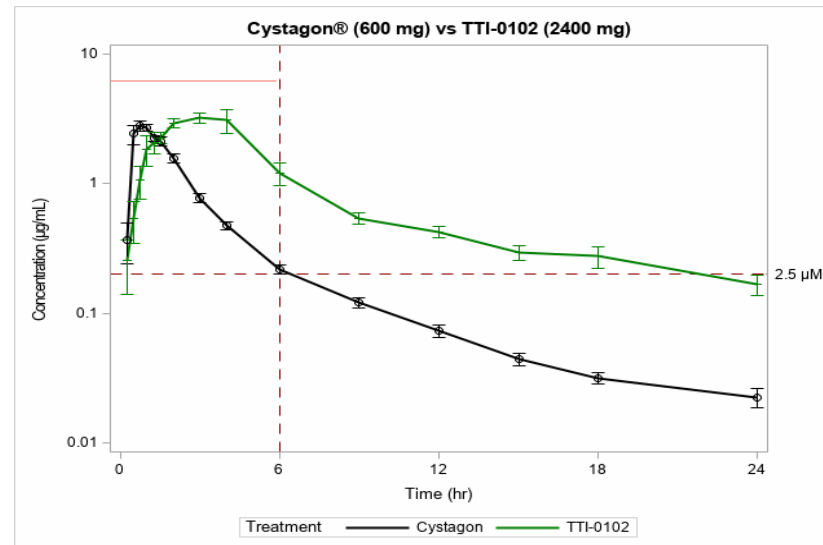


Both transformations occur in a controlled manner, acting as a 'gating metabolic mechanism' and eliminating the spike in cysteamine that is associated with side effects

TTI-0102 Lead Compound

- *TTI-0102* is a proprietary, engineered disulfide that is a precursor to cysteamine
- The '**gating metabolic mechanism**' provides for a 'Controlled Release' of cysteamine

Phase 1 Study (PK/Safety)

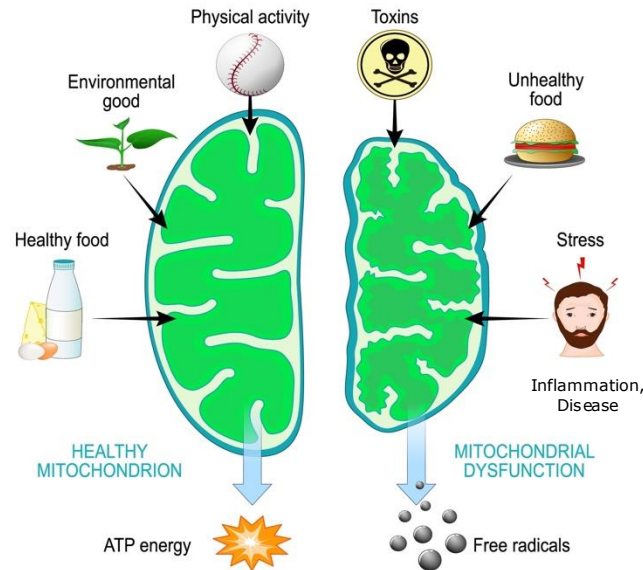


- **TTI-0102 was dosed at 4x** the therapeutic level of Cystagon® (generic cysteamine) in healthy volunteers; it was well-tolerated with no side effects and has potential for once-a-day dosing

Mitochondrial Dysfunction

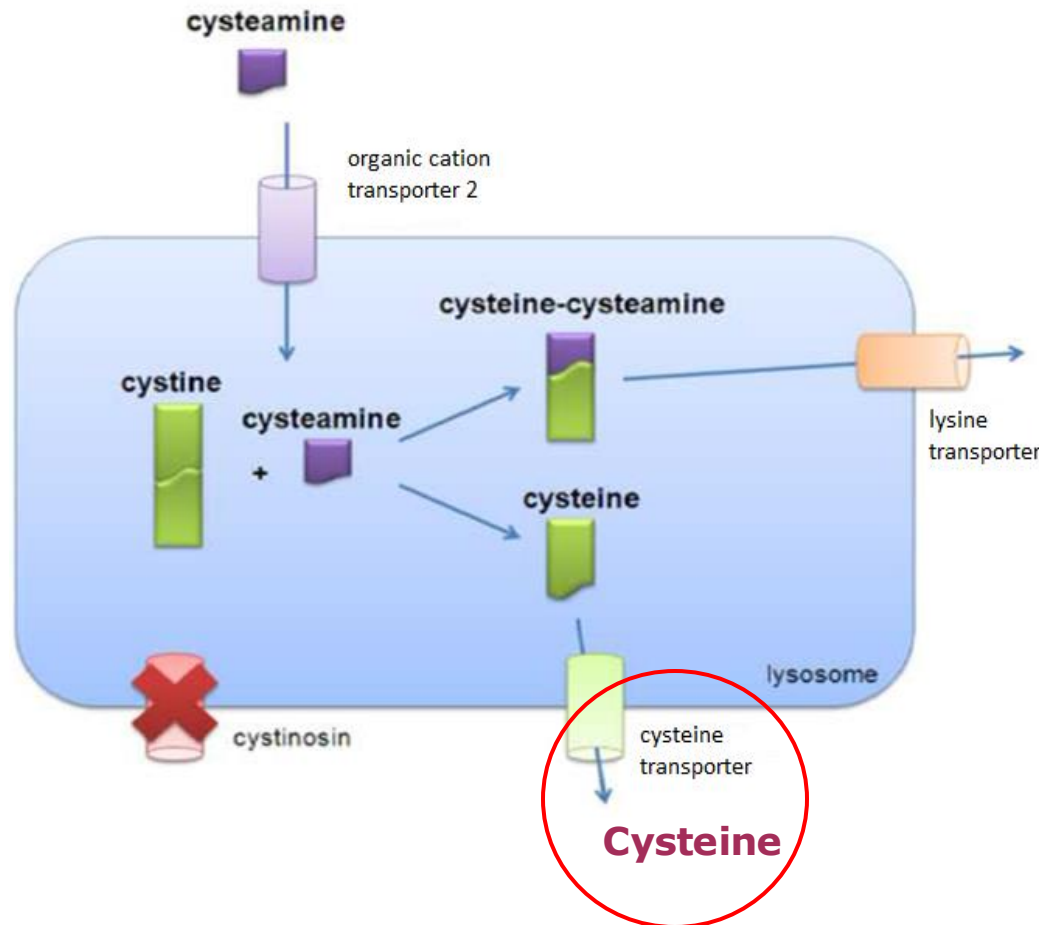
(Oxidative Stress)

Mitochondria's main function is to generate energy necessary to power cells



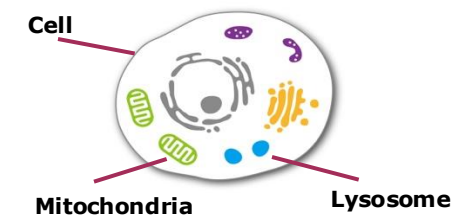
- **Reactive Oxygen Species** (free radicals) are highly reactive molecules, mostly formed in the mitochondria
- **Oxidative stress** occurs when there is too much ROS for antioxidant **defenses like glutathione to neutralize** – which can cause damage to cells/DNA etc.
- ***Oxidative stress is a key feature of inherited mitochondrial and acquired metabolic diseases***

Cysteamine → Cystine Depletion → GSH



Production of Intracellular GSH

- Cysteamine breaks the cystine (*up to 30x concentrated in the lysosome*) into 2 unique thiols that can exit the lysosome, occurs even in patients without cystinosis
- Free cysteine is the limiting factor in the production of intracellular glutathione ("GSH")
- Glutamic Acid + **Cysteine** + Glycine = **GSH**
- GSH is considered the "master" antioxidant, and uniquely enters the mitochondria through a dedicated transporter

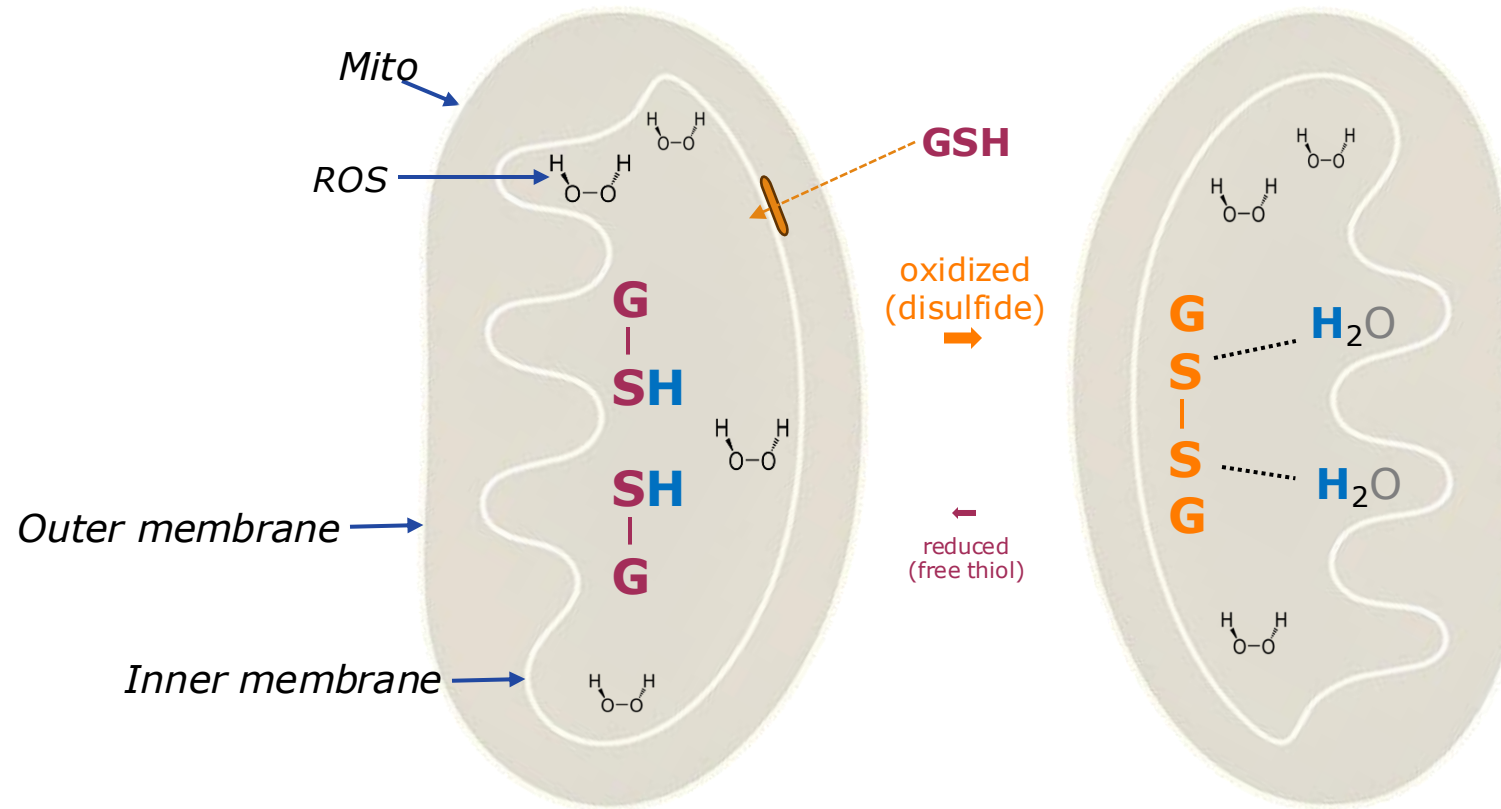


Besouw M - Adapted from et al. Drug Discovery Today, 2013

Thiol/Disulfide - Antioxidation

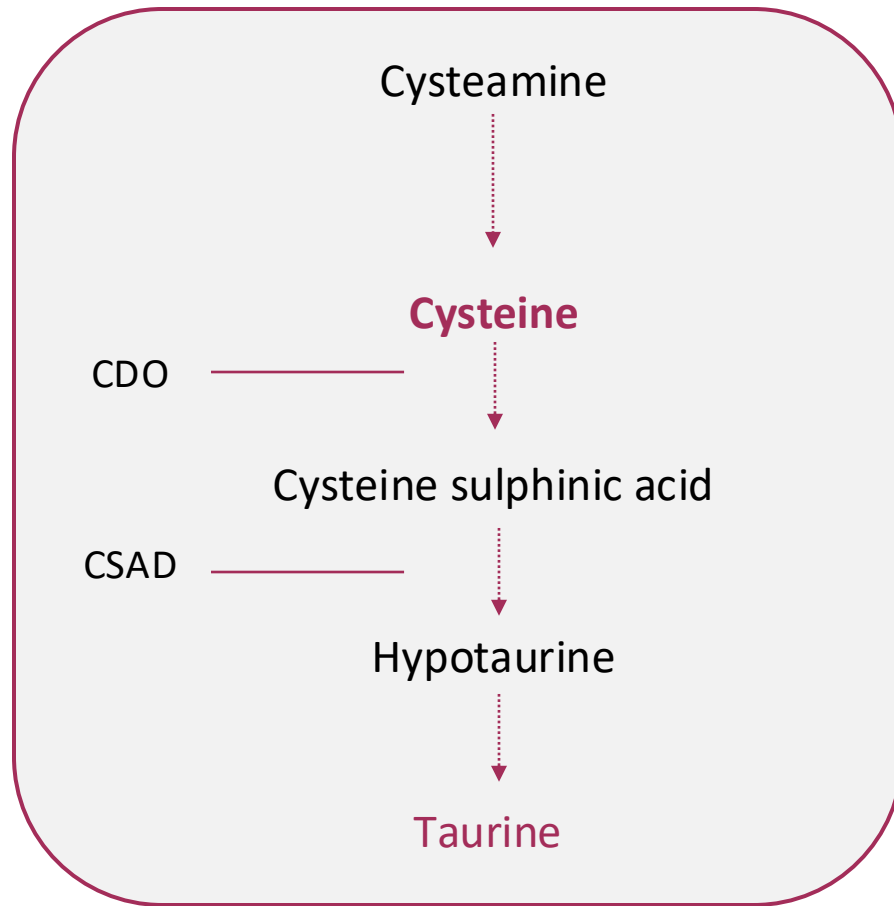
TTI-0102 → **Cysteamine** → **Cysteine** → **Glutathione (GSH)**

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



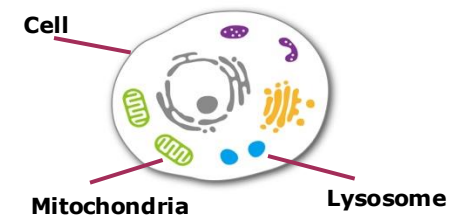
- GSH oxidizes into GSSG – releasing hydrogen that transforms the ROS into harmless water molecules
- **It is critical to supply enough GSH** to neutralize the abundant ROS to restore healthy mitochondrial function

TTI-0102 → Taurine

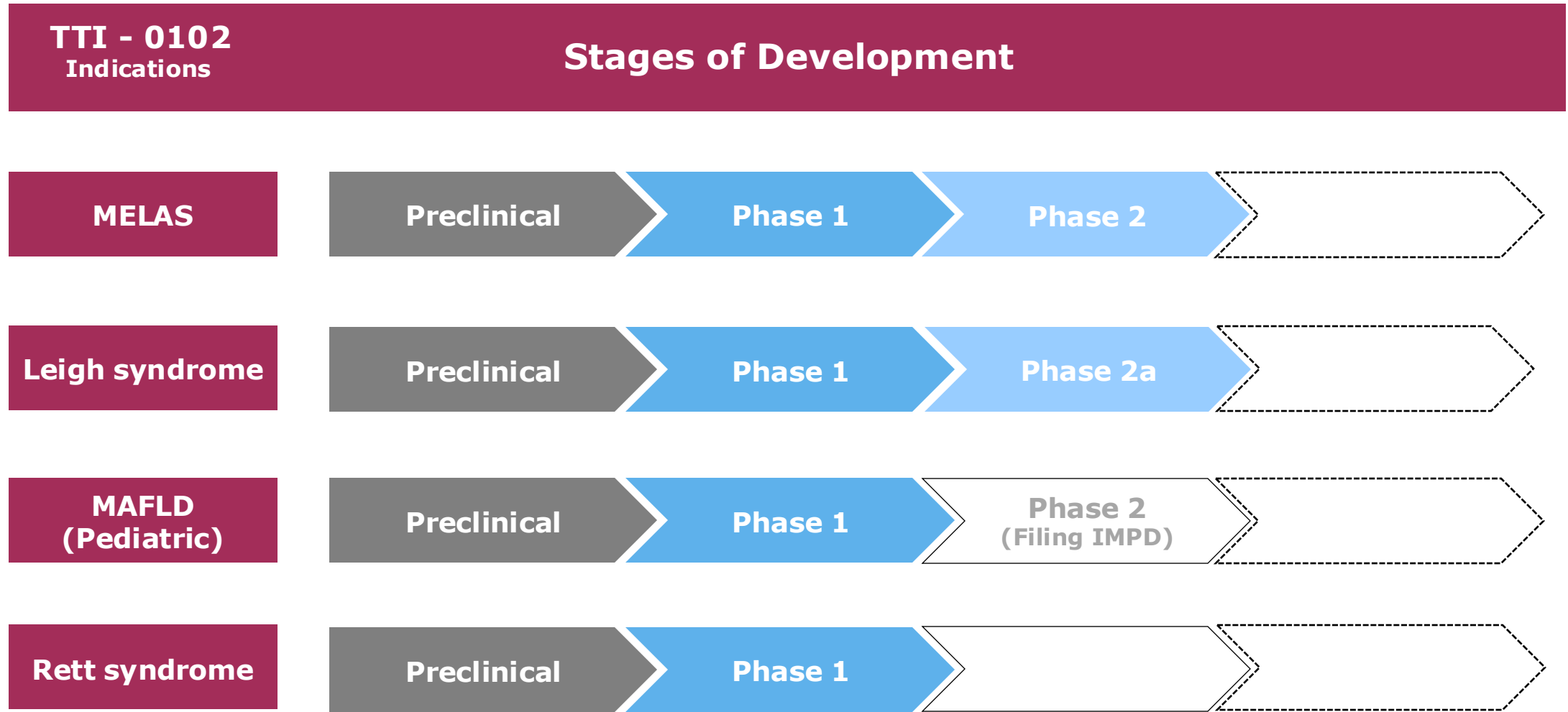


Production of Intracellular Taurine

- 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*
- 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 Multi-Center, 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 followed by 24 weeks of treatment: 28 weeks.
- Primary efficacy endpoint: 12 min walk test; secondary endpoints are significant biomarkers
- *Interim assessment will occur after 9 patients have been treated for 3 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.

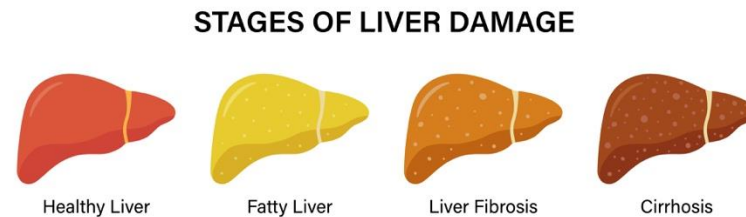
Stage 2:

- 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

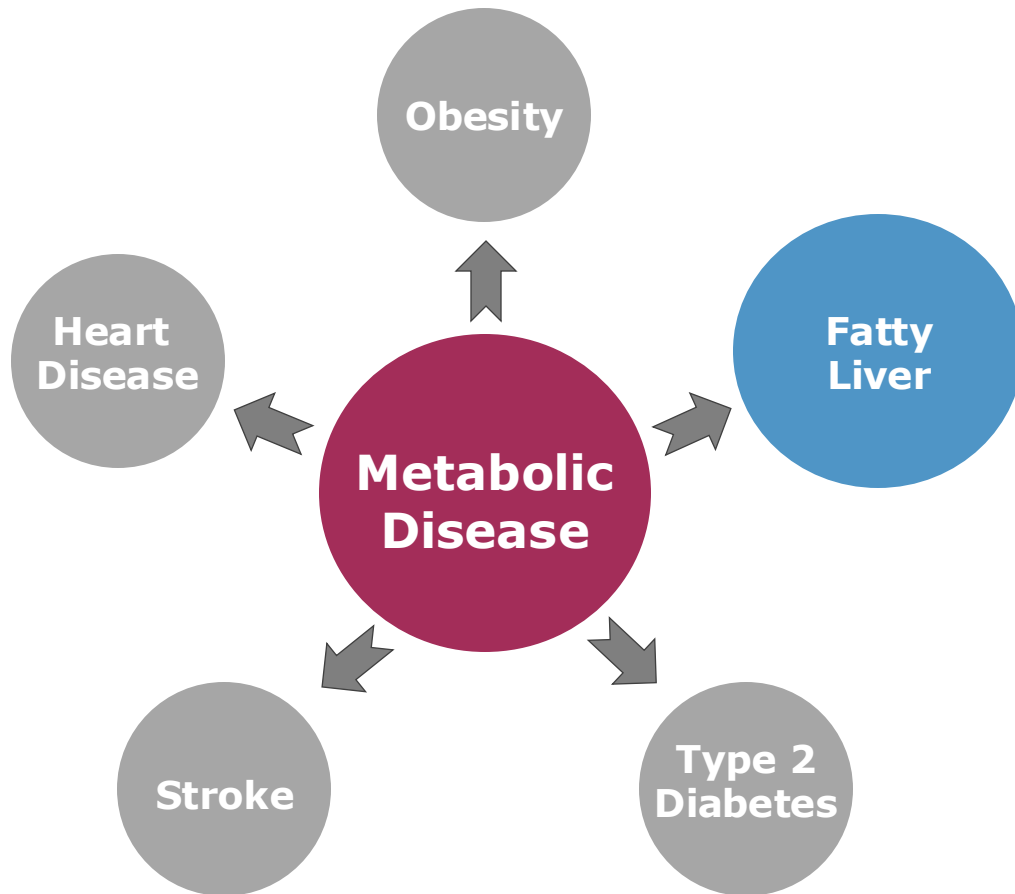
Pediatric MASH

- ***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 (B₅) 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):

<i>MELAS</i>	➡	Initiated Phase 2 trial, Q3/25 interim analysis
Leigh syndrome	➡	Initiate Phase 2 trial H2-2025
Pediatric <i>MASH</i>	➡	Filing IMPD - Phase 2 trial 2025
<i>Rett syndrome</i>	➡	Filing IMPD Phase 2/3 trial

Company Info

Thiogenesis Therapeutics

(TSXV: TTI / OTCQX: TTIPF)

Shares Issued

46.3 million

Shares Fully Diluted

50.3 million

Insiders (36%)

16.7 million

Share Price (06/26/2025)

\$0.74

52 week high/low

\$0.80/C\$0.51

Market Cap.

\$34.3 million

Cash (03/31/2025)

\$3.0 million

Contact

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- Currency in Canadian dollars