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VALUATIONLAB
FINANCIAL ANALYSIS

THIOGENESIS THERAPEUTICS

FOCUS AREA: THIOL-ACTIVE THERAPEUTIC COMPOUNDS TO TREAT MITOCHONDRIAL DYSFUNCTIONS WITH HIGH UNMET MEDICAL NEED

KEY DATA			TSXV: TTI.V
MARKET CAPITALIZATION (CAD MN)	34	**PRICE ON 11 JANUARY 2024**	0.75
ENTERPRISE VALUE (CAD MN)	27	**RISK-ADJUSTED NPV PER SHARE** (CAD) ^^	8.5
ESTIMATED CASH (31 DECEMBER 2023) (CAD MN)	7	**UPSIDE/DOWNSIDE** (%)	1031%
MONTHLY OPERATING EXPENSE (CAD MN)	0.2	**RISK PROFILE**	SPECULATIVE
CASH RUNWAY (YEAR)	INTO Q2 2025	**SUCCESS PROBABILITY LEAD PIPELINE DRUG**	5%
BREAK-EVEN (YEAR)	2026	**EMPLOYEES**	5
FOUNDED (YEAR)	2016	**LISTED** (YEAR)	2022
KEY PRODUCTS:	**STATUS**	**MAJOR SHAREHOLDERS:**	**(%)**
- TTI-0102 (MELAS* - OPRHAN INDICATION)	PHASE II-READY	- MANAGEMENT & INSIDERS	28.2
- TTI-0102 (RETT SYNDROME - ORPHAN INDICATION)	PHASE II-READY	**- FREE FLOAT**	**71.8**
- TTI-0102 (PEDIATRIC NASH** - LARGE INDICATION)	PHASE II-READY	- AVERAGE TRADING VOLUME (30-DAYS)	20'833
- TTI-0102 (SARS***/COVID-19)	UNDER EVALUATION		
UPCOMING CATALYSTS:	**DATE**	**ANALYST(S):**	BOB POOLER
- TTI-0102 (MELAS) - START PHASE IIA POC TRIAL IN EU	Q1 2024		BP@VALUATIONLAB.COM
- TTI-0102 (RETT SYNDROME) - START PHASE II/III POC TRIAL IN EU	MID 2024		+41 79 652 67 68
- TTI-0102 (PEDIATRIC NASH) - START PHASE IIA POC TRIAL IN US	MID 2024		

^^ NOTE: 56.9 MN SHARES USED FOR CALCULATION OF RNPV/SHARE ASSUMING CAD 9 MN (USD 6.6 MN) ADDITIONAL FINANCING TO FUND TTI-0102 POC TRIALS UP TO NEXT VALUE INFLECTION POINTS
* MELAS = MITOCHONDRIAL ENCEPHALOMYOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES; ** NASH = NON-ALCOHOLIC STEATOHEPATITIS; *** SARS = SEVERE ACUTE RESPIRATORY SYNDROME
ESTIMATES AS OF 11 JANUARY 2024 SOURCE: VALUATIONLAB ESTIMATES, THIOGENESIS THERAPEUTICS

A prodrug for mito dysfunction?

TTI-0102: three POCs to prove its blockbuster potential

Thiogenesis Therapeutics (Thiogenesis) is focused on developing proprietary thiol-active (sulfur-based) compounds to treat unmet medical needs of pediatric patients. Lead compound is TTI-0102, a chemically engineered precursor (oral prodrug) to the thiol-active drug cysteamine (branded "Cystagon" by Recordati/Mylan) designed to eliminate its side effects and increase dosing flexibility, with initial clinical development plans in three pediatric diseases, including 1) MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes), 2) Rett syndrome and 3) pediatric NASH (non-alcoholic steatohepatitis), each targeting multi-billion dollar market opportunities with first launches in 2026. TTI-0102 is eligible to use the expedited 505(b)(2) regulatory pathway in the US and the hybrid MAA in the EU, substantially cutting development timelines and costs. With estimated cash and current financial assets of CAD 7 mn (31 December 2023), Thiogenesis should have a cash runway into Q2 2025. We derive a sum-of-parts risk-adjusted (r)NPV value of CAD 8.4 per share, with 61% of the value related to TTI-0102 in MELAS, 27% in Rett syndrome, 9% in pediatric NASH, and 1% in cash. We expect the company to reach breakeven in 2026 (assuming a licensing agreement for pediatric NASH). Thiogenesis' risk profile is Speculative as the company has no product revenues, is loss-making, and is dependent on timely funding to reach profitability.

Key catalysts:

- **Start TTI-0102 POC trial in MELAS (Q1 2024):** marks the first POC trial in its first orphan indication MELAS, with potential peak sales of CAD 4 bn; our success rate increases to 15% (POC) from 5% (phase II-ready) increasing our rNPV by CAD 10.9/share.
- **Start TTI-0102 POC trial in Rett syndrome (mid-2024):** the second orphan indication with no treatment options and estimated peak sales of CAD 1.5 bn; our success rate increases to 15% (POC) from 5%, increasing our rNPV by CAD 4.9/share.
- **Start TTI-0102 POC trial in pediatric NASH (mid-2024):** a large indication affecting millions of children, to be out-licensed on positive POC with estimated peak sales of CAD 4 bn; our success rate increases to 15% (POC) from 5%, increasing our rNPV by CAD 1.6/share.

Investment case, strategy & cash

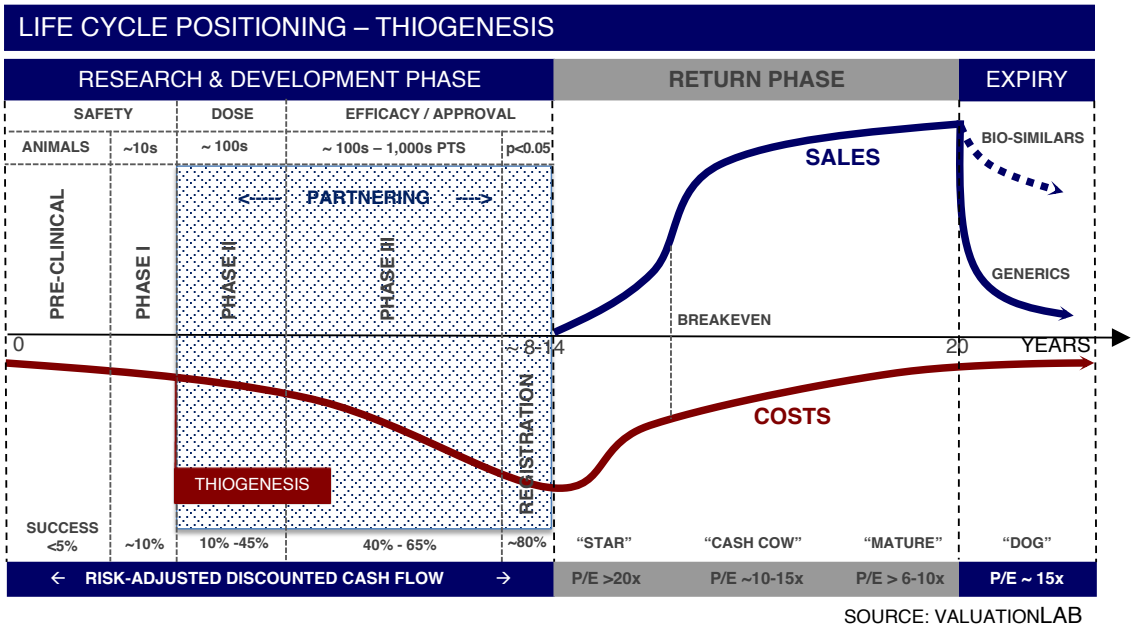
Investment case in a nutshell

Thiogenesis' key driver, TTI-0102, is a "pipeline in a product" for diseases characterized by mitochondrial dysfunction. TTI-0102 will initially target three pediatric indications, MELAS and Rett syndrome, both rare diseases and pediatric NASH, a large indication, all of which lack safe and effective treatments, with estimated global peak sales amounting to CAD 9.6 bn (USD 7 bn) and ample patent life until at least 2037. TTI-0102, being a prodrug of cysteamine, an approved drug to treat the orphan disease cystinosis, is eligible to use the expedited 505(b)(2) regulatory pathway in the US and the hybrid MAA pathway in the EU, substantially cutting development timelines and costs (an estimated CAD 9-13 mn is needed for the three POC trials). Although cysteamine was studied in pediatric NASH (a statistically significant effect was seen in a subgroup of children) and other indications, dose-limiting side effects have prohibited use and approval. As a prodrug, TTI-0102 is designed to reduce or eliminate the side effects and dosing limitations. In the next 9 months, POC trials to establish the use in MELAS, Rett syndrome, and pediatric NASH are expected to start. Substantial equity upside should be unlocked once the POC trials start and positive results are reported.

Based on our detailed bottom-up forecasts for key compound TTI-0102 in its initial first three indications, with ample patent life and market exclusivity, targeting blockbuster markets, we calculate a sum-of-the-parts risk-adjusted NPV of CAD 482 mn or CAD 8.5 per share, conservatively accounting for ~27% share dilution for CAD 9 mn additional capital to fund its clinical development plans up to the next major value inflection points.

Life Cycle Positioning – Speculative

We qualify Thiogenesis' risk profile as Speculative as the company is loss-making, and future revenues depend solely on lead compound TTI-0102, albeit in three indications: MELAS, Rett syndrome, and pediatric NASH targeting multi-billion-dollar opportunities. The company must fund its clinical trials and secure partnerships timely to reach sustainable profits (See Important Disclosures for our Risk Qualification).



SOURCE: VALUATIONLAB

A Canadian biopharmaceutical company focused on developing prodrugs to thiol-active compounds for treating diseases caused by mitochondrial dysfunction.

Thiogenesis Therapeutics Corporation (Thiogenesis) is a Canadian clinical-stage biopharmaceutical company specializing in developing new chemical entities (NCEs) that are prodrugs that act as precursors to thiol-active compounds. Thiols or thiol derivatives are organosulfur compounds that have an R-SH (alkyl sulfhydryl) functional group, where the functional group is responsible for chemical reactions independent of the overall compound. Highly reactive sulfur makes thiols very active in chemistry and creates several promising mechanisms of action that have been studied for decades and have potential as therapeutics for treating diseases caused by mitochondrial dysfunction. Thiogenesis is initially focused on pediatric indications, including mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS), Rett syndrome, and pediatric non-alcoholic steatohepatitis (NASH). Thiogenesis was established in 2018 in San Diego, California, USA, with a staff of 5 senior FTEs and operates as a wholly-owned subsidiary based in San Diego. The company went public through a reverse takeover of Rozdil Capital Corporation, based in Toronto, Canada, where the company was listed on the TSX Venture Exchange in April 2022 with the trading symbol “TTI”.

TTI-0102 was developed to address critical obstacles facing thiol-based drugs

Thiogenesis’ lead compound TTI-0102 is a prodrug disulfide consisting of two thiols that lead to independent cysteamine molecules after ingestion in a naturally controlled manner. Cysteamine is a thiol approved for treating nephropathic cystinosis, a rare genetic lysosomal storage disease in children. There are two branded formulations of cysteamine available in the market: an immediate-release formulation branded “Cystagon” by Mylan / Recordati, approved in 1994 and generically available, and a newer delayed-release formulation branded “Procysbi” by Raptor / Chiesi, approved in 2013, with global sales of USD 210 mn in 2022. In 2016, Horizon (now Amgen) acquired Raptor Pharmaceuticals for USD 800 mn, largely to obtain the rights of Procysbi. Although cysteamine was studied in many diseases, including pediatric NASH, Huntington’s disease, and other indications, at high doses, reaching peak blood concentrations, side effects such as hyperthermia (overheating), lethargy (unusual decrease in consciousness), rash, nausea, vomiting and mouth and body odor prohibited use and approval in these indications. TTI-0102 has been developed to address the critical obstacles facing thiol-based drugs, such as their dosing limitations, strong gastrointestinal side effects, and short half-life (multiple dosing per day).

As a prodrug, TTI-0102 is metabolized into cysteamine after ingestion in a naturally controlled manner; the metabolic process acts as a gating mechanism that eliminates the spike in cysteamine commonly linked to side effects. Its naturally controlled release also allows for increased dosing and has shown the potential to be administered once daily. A phase I dose escalation trial in Australia, completed in Q2 2022, demonstrated that the dosing of TTI-0102 could be increased by 4x the equivalent of immediate-release cysteamine used to treat cystinosis without significant side effects while maintaining a minimum therapeutic level for up to 24 hours, suggesting once-daily dosing, compared to 4x daily dosing for Cystagon (instant-release cysteamine) and 2x daily for Procysbi (delayed-release cysteamine).

First three pediatric orphan indications with global peak sales reaching CAD 9.6 bn

Thiogenesis’ clinical development program for TTI-0102 will initially target three pediatric indications, including MELAS and Rett syndrome, both orphan indications and pediatric NASH, a large indication, all of which lack safe and effective treatments, with estimated

global peak sales amounting to CAD 9.6 bn (USD 7 bn). As a prodrug of cysteamine, TTI-0102 is eligible to use the expedited 505(b)(2) regulatory pathway in the US and its equivalent hybrid marketing authorization application (MAA) pathway in Europe. These pathways provide certain regulatory advantages, as some of the clinical safety data from the active compound may be provided by referencing previous trials not conducted by Thiogenesis (e.g., safety data from Cystagon), substantially cutting development timelines and costs with a smaller number of patients required to establish a positive benefit/risk profile to gain regulatory approval. In the next 9 months, Thiogenesis plans to start phase II proof-of-concept (POC) clinical trials to establish the use of TTI-0102 in MELAS and Rett syndrome first in Europe and pediatric NASH first in the US, with an estimated cost of CAD 9-13 mn (USD 7-10 mn) for all three trials. The company has secured funding for the clinical trials in MELAS and Rett syndrome through the recent private placement of CAD 4.5 mn and cash on hand.

- **MELAS – Orphan indication with the highest peak sales potential of CAD 4 bn**
  MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) is TTI-0102's orphan drug indication with the highest global peak sales potential amounting to CAD 4 bn. MELAS is a rare genetic disorder of the mitochondria that affects the function and development of the brain, causing neurological impairment, lowering oxygen levels in the blood, and seizures with no approved treatments. There are an estimated ~17,000 patients in North America and ~27,000 in Europe, with most patients showing signs by or before the age of 20 years. Current treatment is limited to controlling symptoms, including antiseizure medications, coenzyme Q10 supplementation to increase mitochondrial energy output, L-arginine and L-citrulline to decrease the number of stroke-like episodes, and insulin or metformin to treat diabetes.

  A phase II proof-of-concept (POC) trial is expected to start in France and the Netherlands in H1 2024, with completion roughly one year later and topline results to report shortly after. First sales in the US and EU are expected in 2027. The company plans to apply for early access programs (EAPs) in the EU and the US, which could generate initial, albeit minor, revenues in 2026. We forecast global peak sales for TTI-0102 in MELAS to reach CAD 4 bn (USD 2.9 bn) with commercialization through contract sales organizations (CSOs).

- **Rett syndrome – Fast-to-market orphan indication with peak sales of CAD 1.5 bn**
  Rett syndrome is a fast-to-market orphan indication, with first launches expected in the EU in late 2026. Rett syndrome is a rare genetic mutation of the MECP2 gene, affecting brain development almost exclusively in girls. Infants seem healthy during their first six months, but over time, they rapidly lose coordination, speech, and use of their hands - noticeable abnormal hand movements are a hallmark of the disease. Symptoms may then stabilize for years. There is no cure, but medication, physio- and speech therapy, and nutritional support help manage symptoms, prevent complications and improve quality of life. There are an estimated ~17,000 patients in North America and ~27,000 in Europe

  A phase II/III POC trial of TTI-0102 in girls with Rett syndrome should start in France in mid-2024, with trial completion approximately 18 months later (end 2025) and topline results to report shortly after that. First sales in the EU are expected in late 2026. The company plans to apply for early access programs (EAPs) in the EU and the US, which

could generate early but small revenues in 2026. We forecast global peak sales for TTI-0102 in Rett syndrome to amount to CAD 1.5 bn and commercialization through CSOs.

- **Pediatric NASH – Large indication to be partnered upon positive POC**
  Pediatric NASH (non-alcoholic steatohepatitis), the most severe form of non-alcoholic fatty liver disease (NAFLD), is the first large indication for TTI-0102. NASH is the form of NAFLD in which a child has inflammation of the liver and liver damage, in addition to fat in the liver. The inflammation and liver damage of NASH can cause fibrosis, or scarring, of the liver or may lead to cirrhosis, in which the liver is scarred and permanently damaged with the risk of liver cancer or liver failure and the need for a transplant. Children with specific health problems such as obesity, metabolic syndrome, and type 2 diabetes are more likely to develop NAFLD and NASH. No medicines have been approved to treat NAFLD or NASH in children. Clinical efficacy was seen in a subset group of children with NASH treated with Procysbi (delayed-release cysteamine), providing clinical promise for TTI-0102. There are an estimated 1.5 mn children with NASH in the US and more than 2.5 mn in Europe.

  A phase IIa POC trial in children ages 10-17 with NASH is expected to start in mid-2024, with trial completion expected roughly 18 months later (end-2025), with topline results shortly after. Upon positive POC trial results, Thiogenesis plans to out-license the global rights for (pediatric) NASH to a global biopharmaceutical company for further development and commercialization in return for substantial milestone payments and royalties on sales. The first launches of TTI-0102 in pediatric NASH are expected in 2030, with global peak sales forecast to amount to CAD 4 bn.

Strategy to develop TTI-0102 to an optimal value, then market orphan indications through contract sales organizations (CSOs) and out-license large indications to a major biopharmaceutical company

Thiogenesis' strategy is to develop TTI-0102 to its optimal value in its targeted indications and, in the case of pediatric rare diseases like MELAS or Rett syndrome, to commercialize through contract sales organizations (CSOs) to optimize long-term value and avoid high upfront costs for an own specialist sales infrastructure. Thiogenesis will sell TTI-0102 to its CSOs and book the sales while incurring COGS and small G&A costs to oversee the CSO revenues. Where necessary or advantageous, such as for large indications such as (pediatric) NASH, upon positive POC trial results, the company will seek development and commercialization agreements with a major biopharmaceutical company to reduce R&D costs and generate revenue through R&D funding, upfront, development, regulatory and commercialization milestone payments, and royalties on future sales. This revenue can support the further development of TTI-0102 in MELAS and Rett syndrome and potentially other indications, such as Huntington’s disease.

Cash reach into Q2 2025 boosted by recent CAD 4.5 mn private placement

Thiogenesis should be sufficiently funded into Q2 2025 after securing CAD 4.5 mn in a private placing of 6.0 mn ordinary shares at CAD 0.75 per share in November 2023. As a result, the estimated cash and cash equivalents following the private placement amount to CAD 7.0 mn, which should be sufficient to fund the POC trials of TTI-0102 in MELAS and Rett syndrome up to the next value inflection points. The final trial design of the POC trial in NASH is currently being evaluated with an additional CAD 5-9 mn (USD 4-7 mn) capital needed. To be conservative, we are modeling CAD 9 mn of additional capital to complete the POC trial in pediatric NASH up to its next value inflection point and to cover general

overhead costs. EAPs for TTI-0102 in MELAS and Rett syndrome should lead to early revenues in the single-digit million Canadian dollars, while grants could provide additional non-dilutive funding, reducing the amount of equity needed to be issued. At the same time, a lucrative partnering agreement for pediatric NASH should provide sufficient funds to develop all indications up to approval and launch with breakeven targeted for 2026.

Thiogenesis' key priorities in the next 12-18 months include:

- **Start the proof-of-concept trials of TTI-0102** in its first three pediatric indications, including MELAS (Q1 2024), Rett syndrome (mid-2024), and pediatric NASH (mid-2024).
- **Clearance of the investigational new drug (IND) application for TTI-0102** in COVID-19 (under evaluation), which can be used as a reference IND for development in MELAS, Rett syndrome, and pediatric NASH in the US.
- **Apply for EAPs (Early Access Programs) for TTI-0102** in MELAS and Rett syndrome in Europe, which could lead to early sales in the single-digit million Canadian dollars.
- **Additional single-digit million Canadian dollars capital** to fund the POC trial of TTI-0102 in pediatric NASH up to its next value inflection point (the POC trials for MELAS and Rett have been funded); this may come from non-dilutive grants, early partnering (e.g., regional) or an equity raise, albeit at a likely higher valuation.
- **File for approval** using the expedited 505(b)(2) regulatory pathway in the US and the equivalent hybrid MAA pathway in Europe upon positive POC results of TTI-0102 in MELAS and Rett syndrome.
- **Out-license the rights of TTI-0102 in pediatric NASH** to a (global) partner for further development and commercialization in this large indication, likely upon positive POC results (end 2025).

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CAD 8.5 per share
We derive a sum-of-parts risk-adjusted NPV of CAD 8.5 per share for Thiogenesis, conservatively based on the assumption of a share dilution of 27% (56.9 mn shares) to raise an additional CAD 9 mn (which is purposefully conservative as the company may access grants, receive upfront milestone payments from licensing deals, or raise funds at a significantly higher share price) to fully fund the clinical development program for TTI-0102 up to the next value inflection points, with estimated cash and cash equivalents of CAD 0.1 per share (31 December 2022), overhead of CAD 0.5 per share with a WACC of 13%, consisting of a systemic risk of 9% and a risk-free rate of 4% (10-year Canadian bond yield).

SUM OF PARTS

PRODUCT NAME	INDICATION	PEAK SALES (CAD MN)	PEAK SALES (USD MN)	LAUNCH YEAR	UNADJUSTED NPV/SHARE	SUCCESS PROBABILITY	RISK-ADJUSTED NPV/SHARE (CAD) ^	PERCENTAGE OF TOTAL
TTI-0102	MELAS* (ORPHAN INDICATION)	3'976	2'931	2027	109	5%	5.5	61%
TTI-0102	RETT SYNDROME (ORPHAN INDICATION)	1'545	1'139	2026 (EU)	49	5%	2.5	27%
TTI-0102	PEDIATRIC NASH** (LARGE INDICATION)	4'052	2'987	2030	16	5%	0.8	9%
RPDPR*** VOUCHER (ON US APPROVAL OF TTI-0102)		122	90		3	5%	0.1	2%
ESTIMATED CASH & CASH EQUIVALENTS (31 DECEMBER 2023)		6.7	5		0.1		0.1	1%
TOTAL ASSETS			**7'152**		**178**		**9.0**	**100%**
OVERHEAD EXPENSES					-0.5		-0.5	
NPV/SHARE (CAD)					**177**		**8.5**	
PRICE ON 11 JANUARY 2024							0.75	
PERCENTAGE UPSIDE / (DOWNSIDE)							1031%	

^ NOTE: 56.9 MN SHARES USED FOR CALCULATION OF RNPV/SHARE ASSUMING CAD 9 MN (USD 6.6 MN) ADDITIONAL FINANCING TO FUND TTI-0102 POC TRIALS UP TO NEXT VALUE INFLECTION POINTS
* MELAS = MITOCHONDRIAL ENCEPHALOMYOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES; ** NASH = NON-ALCOHOLIC STEATOHEPATITIS; *** RPDPR = RARE PEDIATRIC DISEASE PRIORITY REVIEW

ESTIMATES AS OF 11 JANUARY 2024 SOURCE: VALUATIONLAB ESTIMATES

TTI-0102's initial indications include:

MELAS (orphan indication) - rNPV of CAD 5.5 per share
MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) is TTI-0102's orphan drug indication with the highest global peak sales potential amounting to CAD 4 bn (USD 2.9 bn) based on our detailed bottom-up financial model. A phase II proof-of-concept (POC) trial with TTI-0102 in patients with MELAS is expected to start in Q1 2024 in France and the Netherlands, with an interim analysis planned 6-9 months after the trial start, with trial completion approximately 1 year later (early 2025). Thiogenesis will apply for EAPs (Early Access Programs) in MELAS, which could generate single-digit million-dollar initial sales. Upon positive POC results, the company will file for approval in the EU using the hybrid MAA regulatory pathway and the 505(b)(2) pathway in the US, with first launches in both regions anticipated in 2027. TTI-0102 will enjoy orphan drug and pediatric market exclusivity of at least 10 + 2 years in the EU and 7 + ½ years in the US from the day of approval. Thiogenesis plans to commercialize TTI-0102 in MELAS through regional and local CSOs (contract sales organizations) with an established sales infrastructure for orphan indications to avoid the costly buildup of its own specialist sales force to maximize long-term profitability. We assume an annual treatment cost per patient of EUR 200,000 (Europe) and USD 350,000 (North America), with peak penetration rates reaching up to 50%, reflecting the lack of therapies and high unmet medical need. We calculate a risk-adjusted (r)NPV of CAD 5.5 per share for TTI-0102 in MELAS with a 5% (phase II-ready) success rate, increasing to 15% upon starting the POC trial in Q1 2024.

Rett syndrome (orphan indication) – rNPV of CAD 2.5 per share
Rett syndrome is expected to be the first approved orphan indication for TTI-0102 with peak sales reaching CAD 1.5 bn. Despite assuming the same pricing as for MELAS, peak sales

are relatively lower due to a significantly lower percentage of patients diagnosed with Rett syndrome. We expect this to rise once TTI-0102 and potentially other treatments are approved. A phase II/III POC trial in patients with Rett syndrome is expected to start in mid-2024, with trial completion approximately 18 months later. The first launches are expected in the EU in late 2026, followed a year later in the US. Upon positive POC trial results, Thiogenesis will follow a similar filing (EU hybrid MAA and US 505(b)(2) regulatory pathway), commercialization (CSOs), and pricing strategy for Rett syndrome as with MELAS (see above). We calculate an rNPV of CAD 2.5 per share with a 5% (phase II-ready) success rate, increasing to 15% once the POC trial starts in mid-2024.

Pediatric NASH (large indication) – rNPV of CAD 0.8 per share

Pediatric NASH (non-alcoholic steatohepatitis), the most severe form of non-alcoholic fatty liver disease (NAFLD), is likely the first large indication for TTI-0102, with global peak sales forecast to amount to CAD 4 bn (USD 3 bn). A phase II POC trial in children aged 10-17 with NASH is expected to start in mid-2024, with an interim analysis 6-9 months after the trial starts and completion approximately 18 months later (end-2025). Upon positive POC trial results, Thiogenesis plans to out-license the rights for (pediatric) NASH to a global biopharmaceutical company for further development and commercialization in return for substantial milestone payments and royalties on sales. The first launches of TTI-0102 in pediatric NASH are expected in 2030, with global peak sales forecast to amount to CAD 4 bn. Given the large number of patients, the annual treatment cost per patient will be substantially lower than for the orphan indications MELAS and Rett syndrome, ranging between EUR 20,000 (Europe) and USD 30,000 (North America). A possible different formulation of TTI-0102 for pediatric NASH could address the substantial difference in pricing. Our rNPV of TTI-0102 in pediatric NASH amounts to CAD 0.8 per share with a 5% (phase II-ready) success rate, increasing to 15% when the POC trial starts in mid-2024.

RPDPR voucher – rNPV of CAD 0.1 per share

Thiogenesis is entitled to a rare pediatric disease priority review (RPDPR) voucher upon US approval of TTI-0102 in MELAS in 2027. The average value of these vouchers, which can be sold freely, is approximately USD 90 mn (CAD 122 mn). Applying the same 5% (phase II-ready) success rate in MELAS, the rNPV amounts to CAD 0.1 per share.

Currently, no value attributed to ROW and other mitochondrial diseases.

We have conservatively not accounted for Rest of the World (ROW) revenues due to the affordability of high-priced orphan drugs in these countries or other potential mitochondrial diseases where TTI-0102 may be effective, which could lead to substantial off-label revenue.

Rest of the World (ROW) revenues: due to the affordability of treatments for orphan indications commanding annual treatment costs in the hundreds of thousands of dollars, out of the reach of most patients and healthcare insurers, we have conservatively excluded forecasts for TTI-0102 in the Rest of the World. Sales for countries such as Japan, Australia, New Zealand, China, and some Asian Pacific or Middle Eastern countries could add to our TTI-0102 forecasts in all indications.

Other mitochondrial diseases: It is estimated that genetic mitochondrial disease affects approximately 65,000 people in the US alone. MELAS is the first and largest mitochondrial disease that is targeted by TTI-0102, affecting roughly 15,000 patients, or ~23% of the estimated mitochondrial patients in the US. If approved for MELAS, TTI-0102 would have promise in other mitochondrial diseases resulting from mitochondrial DNA mutations such

as **MERRF** (Myoclonic Epilepsy with Ragged Red Fibers) associated with myoclonic seizures, muscle weakness, ataxia (loss of muscle control in arms and legs), and the presence of ragged red fibers; **Leigh Syndrome**, a severe neurological disorder affecting infants and children with progressive loss of mental and motor abilities along with weakness and respiratory problems; **NARP** (Neuropathy, Ataxia and Retina Pigmentosa) characterized by a range of symptoms including peripheral neuropathy, ataxia, and vision problems like retinitis pigmentosa; **Kearns-Sayre Syndrome**, a rare condition characterized by onset before age 20 with progressive external ophthalmoplegia (eye muscle paralysis), pigmentary retinopathy and heart block; and **Mitochondrial Depletion Syndrome**, which involve a significant reduction in mitochondrial DNA content leading to impaired mitochondrial function affecting various organs and systems resulting in severe, multisystemic manifestations.

With no effective treatments available, this could lead to substantial off-label use – the use of a drug not approved for a specific disease – of TTI-0102 in these patients, roughly 3 times the number of MELAS patients. We conservatively do not include off-label use of TTI-0102 in our forecasts.

Sensitivities that can influence our valuation

Funding risk: Thiogenesis cash should reach into Q2 2025 with an estimated CAD 5-9 mn (USD 4-7 mn) needed to fund its clinical development plans for TTI-0102 in pediatric NASH (the POC trials in MELAS and Rett syndrome have been funded) up to its next value inflection point. A lucrative partnering agreement for the global rights of TTI-102 in pediatric NASH, a large indication, in return for substantial upfront, development and commercialization milestone payments and royalties on sales, could fund the further development of TTI-0102 in MELAS, Rett syndrome, and other likely orphan indications. EAPs could also add to the revenue stream.

Development risk: Positive results were seen in the randomized phase IIb "CyNCh" dosing trial in a subset group of children with NASH who were treated with adequately high doses of Procysbi (delayed-release cysteamine). TTI-0102 can be given once daily at higher doses with fewer and lower spikes (cause of side effects) than Procysbi, providing clinical promise in pediatric NASH. MELAS and Rett syndrome lack similar proof-of-concept (POC) with cysteamine treatment as pediatric NASH. We conservatively use a historical 5% (phase II-ready) success rate for all three indications, which will increase to 15% upon the start of the POC trials.

Regulatory risk: Upon positive results in the targeted primary endpoints, regulatory approval should be swift, with a lack of effective treatments for all three indications. With TTI-0102 being a prodrug, it may use the EU hybrid MAA and US 505(b)(2) regulatory pathway referencing clinical safety data of Cystagon and Procysbi.

Pricing and reimbursement: Following EMA and FDA approval, TTI-0102 must be priced and reimbursed by healthcare providers. In the US, pricing and reimbursement are quite straightforward. In the EU, pricing and reimbursement occur on a country-by-country base, leading to different pricing and reimbursement and potential market launch delays. Pricing and reimbursement may differ from our forecasts.

Commercialization risk: Thiogenesis' revenues and earnings for TTI-0102 are entirely dependent on CSOs (contract sales organizations) for orphan indications and its commercialization partner(s) for large indications such as pediatric NASH to position and market the compound in each indication and the different regions successfully. Revenues and terms of the agreements, as well as the timing, may differ from our forecasts.

Patent and market exclusivity: Thiogenesis has a robust patenting strategy for TTI-0102, providing protection until at least 2037 (excluding potential patent term extensions) with Composition of Matter (COM) patent applications for the mixed disulfide (WO2017161318 – compositions for controlled-release of cysteamine and systemic treatment of cysteamine disorders) and Method of Use (MOU) patent applications (WO2019060634 – methods for the treatment of cysteamine sensitive disorders) in major markets, such as Europe and the US. Thiogenesis also has a COM/MOU patent (PCT/US21/25070) for TTI-0102 in the treatment of betacoronavirus infections, including those infections that cause COVID-19. Additionally, TTI-0102 should enjoy 10 + 2 years of orphan and pediatric market exclusivity upon approval in the EU and 7 + ½ years in the US for pediatric orphan indications such as MELAS and Rett syndrome.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT ON RNPV/SHARE
2023					
Q1	TTI-0102	MELAS *	PREPARATION IMPD/CTA FILING	PHARMALEX (ACQUIRED BY AMERISOURCEBERGEN) WAS ENGAGED TO PREPARE AND SUPPORT THE IMPD (INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER) FOR THE CTA (CLINICAL TRIAL APPLICATION) FILING IN THE EU (THE EQUIVALENT OF AN INVESTIGATIONAL NEW DRUG (IND) APPLICATION IN THE US) TO START A PHASE II CLINICAL TRIAL IN FRANCE AND THE NETHERLANDS TO TREAT MELAS * PATIENTS	
MAR			KEY PATENT ISSUED IN US	US KEY PATENT "METHODS FOR THE TREATMENT OF CYSTEAMINE SENSITIVE DISORDERS" (NUMBER US 11,612,576 B2) WAS ISSUED COVERING THE ADMINISTRATION OF A DISULFIDE CONVERTIBLE TO CYSTEAMINE IN VIVO, WHICH MAKES IT A PRO DRUG ELIGIBLE TO FILE UNDER THE SECTION 505(B)(2) PATHWAY AND THE HYBRID MEDICINAL PRODUCT APPLICATION IN THE EU	
Q2	TTI-0102	MELAS, RETT SYNDROME, PEDIATRIC NASH **	SECOND-GENERATION FORMULATION	START DEVELOPMENT OF A SECOND-GENERATION FORMULATION OF TTI-0102 TO BE ADMINISTERED IN A MORE STABLE TABLET OR SACHET INSTEAD OF THE CURRENT POWDER FORMULATION BY WUXI STA, THE LEAD MANUFACTURER OF TTI-0102	
10 MAY			FY 2022 RESULTS & CORPORATE UPDATE	FY 2022 RESULTS - R&D: CAD 1.1 MN (2021: CAD 1.4 MN), G&A: CAD 0.9 MN (2021: CAD 0.3 MN), NET LOSS: CAD 3.9 MN (2021: CAD 1.2 MN); CASH & CASH EQUIVALENTS: CAD 6.2 MN (31 DECEMBER 2022)	
5 OCT	TTI-0102	MELAS	IMPD APPLICATION FILING	EUROPEAN IMPD (INVESTIGATIONAL MEDICAL PRODUCT DOSSIER) APPLICATION FILED FOR A PHASE IIA POC (PROOF-OF-CONCEPT) WITH TTI-0102 FOR THE TREATMENT OF MELAS IN FRANCE AND THE NETHERLANDS	
20 NOV			CAPITAL RAISE	CAD 4.5 MN CAPITAL RAISED IN A NON-BROKERED PRIVATE PLACEMENT THROUGH THE ISSUANCE OF 6 MN COMMON SHARES AT A PRICE OF CAD 0.75/SHARE; CLOSING SUBJECT TO REGULATORY APPROVALS ROUGHLY ONE MONTH LATER; AN ESTIMATED CAD 9 MN NEEDED TO FUND CLINICAL DEVELOPMENT PLANS OF TTI-0102 IN MELAS, RETT SYNDROME, AND PEDIATRIC NASH UP TO THE NEXT VALUE INFLECTION POINTS	
Q4		RETT SYNDROME, PEDIATRIC NASH	SECOND-GENERATION FORMULATION	A NEW TABLET FORMULATION OF TTI-0102 WAS DEVELOPED WITH LEAD SUPPLIER WUXI STA; THIS NEW TABLET FORMULATION WILL BE USED INSTEAD OF THE CURRENT POWDER FORMULATION FOR CLINICAL TRIALS IN RETT SYNDROME AND PEDIATRIC NASH; ADDITIONAL INTELLECTUAL PROPERTY (IP) WAS FILED TO EXTEND PATENT PROTECTION OF THIS NEW SALT	
Q4	TTI-0102	MELAS	PHASE IIA POC TRIAL - CLEARANCE	REGULATORY CLEARANCE PHASE IIA PROOF-OF-CONCEPT (POC) TRIAL IN MELAS PATIENTS IN FRANCE/THE NETHERLANDS	
~20 DEC			CAPITAL RAISE CLOSED	CAD 4.5 MN CAPITAL RAISE CLOSED AFTER RECEIPT OF ALL NECESSARY REGULATORY APPROVALS	
2024					
Q1	TTI-0102	MELAS	PHASE IIA POC TRIAL - START	START PHASE IIA POC TRIAL IN MELAS PATIENTS IN FRANCE AND THE NETHERLANDS WITH THE POWDER FORMULATION OF TTI-0102; PRIMARY ENDPOINT IS IMPROVEMENT IN 12 MINUTE WALK TEST (12MWT); INTERIM ANALYSIS PLANNED 6-9 MONTHS AFTER START; TRIAL COMPLETION APPROXIMATELY 1 YEAR LATER (Q1 2025); TOPLINE RESULTS TO FOLLOW SHORTLY AFTER	+ CAD 10.9
Q1	TTI-0102	PEDIATRIC NASH	IND FILING	FDA INVESTIGATIONAL NEW DRUG (IND) FILING FOR A PHASE II POC TRIAL IN PEDIATRIC NASH TO BE CONDUCTED IN THE US	
MID	TTI-0102	PEDIATRIC NASH	PHASE IIA POC TRIAL - START	START PHASE IIA POC TRIAL IN PEDIATRIC NASH PATIENTS USING THE NEW TABLET FORMULATION; PRIMARY ENDPOINT IS THE CHANGE IN PERCENTAGE OF HEPATIC STEATOSIS (FATTY LIVER DISEASE) FOLLOWING A CERTAIN TREATMENT PERIOD; INTERIM ANALYSIS PLANNED 6-9 MONTHS AFTER START; TRIAL COMPLETION APPROXIMATELY 18 MONTHS LATER (END 2025); TOPLINE RESULTS TO FOLLOW SHORTLY AFTER	+ CAD 1.6
MID	TTI-0102	RETT SYNDROME	PHASE IIB/III POC TRIAL - START	START PHASE II/III POC TRIAL IN RETT SYNDROME PATIENTS IN FRANCE USING THE NEW TABLET FORMULATION; PRIMARY ENDPOINT IS IMPROVEMENT OF BEHAVIORAL DISORDERS MEASURED BY THE ABC (ABERRANT BEHAVIORAL CHECKLIST) SCALE; TRIAL COMPLETION APPROXIMATELY 18 MONTHS LATER (END 2025); TOPLINE RESULTS TO FOLLOW SHORTLY AFTER	+ CAD 4.9
H2	TTI-0102	MELAS	PHASE IIA POC TRIAL - INTERIM RESULTS	INTERIM (FUTILITY) RESULTS DETERMINE TRIAL CONTINUATION	
Q4	TTI-0102	MELAS	PHASE IIA POC TRIAL - COMPLETION	COMPLETION EU PHASE II POC TRIAL IN MELAS PATIENTS IN FRANCE/NETHERLANDS - TOPLINE RESULTS TO FOLLOW SHORTLY AFTER	+ CAD 16.3
Q4	TTI-0102	MELAS	EARLY ACCESS PROGRAM (EAP)	APPLY FOR AN EARLY ACCESS PROGRAM (EAP) FOR MELAS PATIENTS IN FRANCE WHICH COULD GENERATE INITIAL SALES FOR TTI-0102 FROM 2025	
Q4	TTI-0102	RETT SYNDROME	PHASE IIB/III POC TRIAL - INTERIM RESULTS	INTERIM RESULTS EXPECTED 6-9 MONTHS AFTER TRIAL START	

* MELAS = MITOCHONDRIAL ENCEPHALOMYOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES; ** NASH = NON-ALCOHOLIC STEATOHEPATITIS

ESTIMATES AS OF 11 JANUARY 2024

SOURCE: VALUATIONLAB ESTIMATES, THIOGENESIS THERAPEUTICS

Technology & Pipeline

Technology - Unlocking the full potential of cysteamine-based drugs.
Thiogenesis is focused on developing novel thiol-active therapeutic compounds to treat pediatric and orphan diseases with unmet medical need. Thiol-active compounds, such as cysteamine, are molecules that contain a sulfur (S) atom bonded to a hydrogen (H) atom, known as a thiol-group (-SH). These compounds are important in various biological and chemical processes because they can participate in reactions that involve the transfer of electrons, making them essential in processes like redox reactions and protein structure. Thiol-active compounds include molecules like cysteine and glutathione, which play critical roles in cellular functions and antioxidant defenses. Cysteamine-based drugs have potential as therapeutics in many mitochondrial, metabolic, and central nervous system (CNS) diseases. These compounds are known to have powerful antioxidant properties as well as other therapeutic benefits. However, their use is limited due to dose-limiting side effects and their short half-life requiring frequent dosing. It is believed that cysteamine is the thiol or -SH group compound with the most potential for new therapeutic applications, but only if the challenges of its short half-life and side effects can be improved upon. Thiogenesis lead compound is TTI-0102, a so-called prodrug or precursor of cysteamine, specifically designed to avoid the drawbacks of cysteamine and unlock its full therapeutic potential.

Thiogenesis management has extensive experience working with cysteamine from their senior roles in Raptor Pharmaceuticals, the developer of Procysbi, a delayed-release formulation of cysteamine approved for cystinosis, a rare genetic lysosomal storage disease. In 2016, Raptor was acquired by Horizon Therapeutics (now Amgen) for USD 800 mn (USD 1.1 bn), largely to acquire the rights of Procysbi (global sales of USD 210 mn (CAD 285 mn) in 2022).

Thiogenesis' technology platform and strategy are based on three main pillars, cysteamine, prodrug, and orphan drug, which we will discuss in detail below:

1) CYSTEAMINE – a broad range of indications with high unmet medical need

Clinical use: Cysteamine is a thiol approved for cystinosis, a rare genetic lysosomal storage disease, with two approved formulations, "Cystagon" (immediate-release) in 1994, now generically available, and "Procysbi" (delayed-release) in 2013.

Clinical promise: Potential in diseases caused by mitochondrial dysfunction such as MELAS, pediatric NASH, and rare childhood diseases such as Rett syndrome.

Clinical efficacy: Positive efficacy in pediatric NASH was established in a subset group of (adequately dosed) children in the phase IIb "CyNCh" dosing trial with Procysbi.

Cysteamine – a broad range of indications with high unmet medical need
Sulfur is the seventh most abundant element in the human body and plays a central role in the structure and function of thousands of biologically important molecules. Thiols are compounds that contain a sulfur (S) atom bonded to a hydrogen (H) atom, known as a thiol-group (-SH), and are one of the most biologically important subcategories of sulfur-

containing molecules because of their versatile chemistry. Functional groups are the reactive units of molecules in organic chemistry.

The compound cysteamine, which is a thiol with an active functional -SH group, has multiple mechanisms of action with potential therapeutic benefits, which have been widely studied for several decades. Historically, cysteamine was studied as a shield against radiation poisoning in the 1950s. In the 1970s, it was studied as a therapeutic for sickle cell anemia and later to protect against paracetamol toxicity. In the 2000s, cysteamine was studied in pediatric NASH and Huntington's disease, among several other indications. None of these applications were eventually commercialized.

Cysteamine is a well-studied thiol with an active functional R-SH group, giving it multiple mechanisms of action with potential therapeutic benefits, including:

- Increases the amino acid cysteine, which is a precursor to the important anti-oxidant glutathione - the lack of cysteine is usually the limiting factor in the human production of glutathione.
- Is a precursor to the amino acid taurine (and its intermediary hypotaurine), which has cytoprotective properties and other benefits in the organization of the mitochondria.
- Binds to the ACE2 receptor, giving it important anti-viral properties.
- Is an anti-inflammatory, potentially inhibiting cytokine storm in viral disease.
- Acts as a mucolytic (mucus thinner).
- Provides copper chelation, which prevents harmful copper accumulation in cells.
- Promotes the production of brain-derived neurotropic factor (BDNF), a protein important in nerve growth and brain function.

Clinical use – approved for cystinosis; other uses hampered by side effects

Cysteamine bitartrate formulations were approved in 1994, including an immediate-release formulation branded "Cystagon" by Mylan / Recordati (now generically available), and in 2013, a delayed-release formulation branded as "Procysbi" by Raptor / Chiesi (sales of USD 210 mn (CAD 285 mn) in 2022) - both for the treatment of cystinosis. Cystinosis is a rare genetic, life-threatening lysosomal storage disease in children where the transporter for the disulfide cystine is not functioning, and the resulting buildup of cystine in the cells is toxic. When cysteamine is introduced into the cells, it converts the cystine into two different molecules that are both able to leave the cells via a different functioning transporter, exemplifying the metabolic versatility of utilizing compounds with -SH bio-active drugs.

Cysteamine has long been considered a promising drug candidate for several other indications, but its commercial expansion has been constrained due to its poor side-effect profile, restrictions on dosing, and the resulting lack of compliance. Both Cystagon and Procysbi cause unpleasant side effects at peak blood concentrations. These include halitosis (bad-smelling breath), body odor, nausea/vomiting, fatigue, and gastrointestinal pain.

Clinical promise – in diseases caused by mitochondrial dysfunction and more

Thiogenesis lead compound TTI-0102, a prodrug of cysteamine, has the potential of reducing or eliminating many of these side-effects thereby allowing the full potential for cysteamine-based drugs to be realized. It was designed to address the obstacles that hinder thiol-active drugs, such as short elimination half-lives, discomforting side effects, and dosing limitations, any of which can lead to compliance issues. The company will initially focus on TTI-0102's potential to treat diseases caused by mitochondrial dysfunction, such as MELAS

and pediatric NASH, and Rett syndrome, another rare childhood genetic disease. There are several other potential applications that could be targeted for improved cysteamine-based compounds, including Huntington's disease, Parkinson's disease, traumatic brain injury, and COVID-19 infection.

Clinical promise – positive efficacy was seen in a subgroup of children with NASH
In 2016, a US National Institutes of Health (NIH)-sponsored double-blind, placebo-controlled, randomized phase IIb dosing trial, dubbed "CyNCh" of 169 children aged 8 to 17 years with NASH who were treated with twice-daily Procysbi (delayed-release cysteamine) or placebo missed its primary endpoint, the improvement of liver histology after 52 weeks of treatment (p=0.34). Importantly, in a subgroup of patients, including children < 13 years and children with a baseline weight of < 68 kg, a statistically significant improvement in liver histology was seen after 52 weeks of Procysbi treatment, with a p-value of 0.04 for children < 13 years and a p-value of 0.005 in children with a baseline weight of < 68 kg. These younger and lighter children received a relatively higher (adequate) dose of Procysbi than the older and heavier cohort of children, who were likely underdosed. This resulted in the overall treatment group missing its primary endpoint. Therefore, we believe treating children with NASH with TTI-0102, a prodrug of cysteamine that offers a naturally controlled release of cysteamine at higher doses and increased time of therapeutic exposure, has clinical promise.

2) PRODRUG – faster regulatory timelines, lower development costs & risk, new IP

New intellectual property (IP): The new prodrug formulation allows for additional patent protection, including Compositions of Matter (COM) and Methods of Use (MOU) patents, providing TTI-0102 patent protection until at least 2037 (excluding potential patent term extensions).

Naturally controlled-release: TTI-0102 avoids cysteamine spikes linked to side effects and lead to dosing limitations; can be given at 4x higher doses than Cystagon; ability to reach an effective (high) dose of cysteamine without major side effects; once-daily dosing likely.

Expedited regulatory pathway: As a prodrug, TTI-0102 is eligible for the expedited 505(2)(b) pathway in the US and the hybrid MAA pathway in the EU, resulting in faster development timelines and substantially lower development costs and risk.

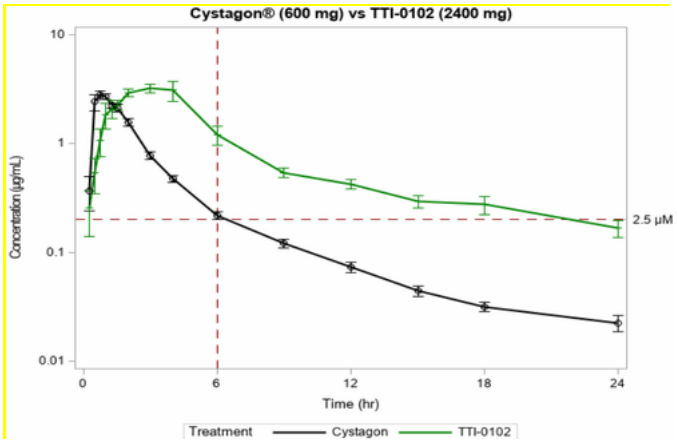
Prodrug – faster regulatory timelines, lower development costs & risk, new IP
A prodrug is a pharmacologically inactive compound that is converted into an active drug inside the body through metabolic or chemical processes. Essentially, it is a precursor to the active form of the drug. The conversion usually occurs after ingestion, either through enzymatic processes in the body or through spontaneous chemical processes. Prodrugs are designed to improve various aspects of drug delivery, absorption, distribution, and targeting. They can offer advantages such as enhanced bioavailability, reduced side effects, improved stability, and better patient compliance.

New intellectual property – provides protection in the major markets until at least 2037
Thiogenesis has synthesized novel compounds that are New Chemical Entities (NCEs) specifically designed as prodrugs or precursors to thiols. Its lead compound, TTI-0102, is an asymmetric disulfide made up of two thiols that have been synthesized with granted

compositions of matter (COM) patents in the major markets, providing protection until at least 2037 (excluding potential patent term extension)

Naturally controlled-release – given at doses 4x higher than Cystagon and 1x daily
TTI-0102 was created to address the obstacles that hinder thiol-active drugs such as Cystagon (immediate-release cysteamine) and Procysbi (delayed-release cysteamine); they typically have short elimination half-lives, discomforting side effects, and dosing limitations, any of which can lead to compliance issues. As a prodrug, TTI-0102 is metabolized into cysteamine after ingestion in a naturally controlled manner. The metabolic process acts as a gating mechanism that slows down the rate of metabolism of TTI-0102, eliminating the spike in cysteamine commonly linked to side effects and increases the time of therapeutic exposure. Eliminating the spike in cysteamine has the potential to reduce its side effects and provide increased dosing flexibility significantly.

In a comparative dose escalation trial on healthy volunteers in Australia, TTI-0102 was dosed up to 4x the cysteamine equivalent of Cystagon (immediate-release). Trial results with TTI-0102 (2,400 milligrams of cysteamine equivalent) demonstrated that TTI-0102 did not exceed the peak levels of cysteamine that were measured in plasma with Cystagon (600 milligrams); only mild body odor was observed at the highest level of dosing of TTI-0102 (2,400 milligrams); a minimum therapeutic availability of cysteamine was maintained for a period of 24 hours, offering the potential of once-daily dosing and improved patient compliance.



Source: Thiogenesis Therapeutics

Expedited regulatory pathways - save substantial time and money for clinical trials
The Food and Drug Administration (FDA) and the European Medicines Agency (EMA) govern Thiogenesis' clinical trials in their respective jurisdictions. As a prodrug, TTI-0102 is eligible to use the expedited 505(b)(2) regulatory pathway in the US and its equivalent hybrid MAA (marketing authorization application) pathway in Europe. These pathways provide certain regulatory advantages, as some of the clinical safety data from the active compound may be provided by referencing previous studies not affiliated with Thiogenesis (such as safety data from Cystagon), which can save substantial time and money in progressing to human efficacy trials.

3) ORPHAN DRUG – a fast-to-market approach with many advantages:

Incentives for development / reduced development costs: Government incentives such as research grants, tax credits, smaller trial patient populations, and extended market exclusivity are provided to offset developing drugs for small patient populations.

Faster regulatory process: Regulators provide accelerated review processes and approval pathways for orphan drugs to reach patients more quickly, prolonging the effective return/lifetime of a product.

High-margin products: To offset development costs for a small patient group, orphan drugs are typically high-priced, reimbursed drugs with only a small specialist sales force needed to target prescribers and patients adequately.

Market exclusivity: The EU provides 10-year market exclusivity, and the US 7-year market exclusivity for orphan drugs upon the day of approval. This is extended by 2-year and 6-month pediatric market exclusivity when the drug is approved for children.

Orphan drug – a fast-to-market approach with many advantages

Thiogenesis is focused on developing TTI-0102 in pediatric orphan (rare disease) indications that lack effective therapies in a fast-to-market strategy. The company plans to start clinical POC trials for TTI-0102 first in the EU for orphan indications such as MELAS and Rett syndrome in 2024. Orphan Drug Designation (ODD) is available for drugs that treat a rare disease or condition. In the US, an orphan disease is defined as less than 200,000 patients diagnosed in the US, and in the EU defined as affecting not more than 5 in 10,000 people. The ODD's purpose is to provide incentives for drug makers to develop drugs for rare indications that otherwise might not be developed due to the cost of traditional drug development. In addition to potential tax incentives and regulatory assistance, the key incentive is ODD market exclusivity for an approved drug. This is 10 years in the EU and 7 years in the US from the day of approval. Approval in children adds 2 years pediatric market exclusivity in the EU and 6 months in the US. TTI-0102 was granted ODD for Rett syndrome in the EU by the EMA in 2021.

Pipeline – Targeting rare and common pediatric disorders with unmet medical need

With multiple mechanisms of action, TTI-0102 has the potential as a therapeutic for a variety of applications, ranging from orphan indications such as mitochondrial diseases (MELAS), Rett syndrome, Huntington's disease, and cystinosis to large indications such as (pediatric) NASH, Parkinson's disease, and COVID-19 infection (under evaluation).

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	PEAK SALES
TTI-0102	ALKYTHIOLS - ORAL PRODRUG (PRECURSOR) TO CYSTEAMINE	MELAS * (ORPHAN INDICATION)	PHASE II-READY	2027	CONSTRACT SALES ORGANIZATION (CSO)	CAD 4 BN
TTI-0102	ALKYTHIOLS - ORAL PRODRUG (PRECURSOR) TO CYSTEAMINE	RETT SYNDROME (ORPHAN INDICATION)	PHASE II-READY	2026	CONSTRACT SALES ORGANIZATION (CSO)	CAD 1.5 BN
TTI-0102	ALKYTHIOLS - ORAL PRODRUG (PRECURSOR) TO CYSTEAMINE	PEDIATRIC NASH ** (LARGE INDICATION)	PHASE II-READY	2030	DEVELOPMENT & COMMERCIALIZATION PARTNER	CAD 4 BN
TTI-0102	ALKYTHIOLS - ORAL PRODRUG (PRECURSOR) TO CYSTEAMINE	INFECTIOUS DISEASES (SARS***, COVID-19 & VARIANTS)	UNDER EVALUATION	TBD	TBD	TBD

* MELAS = MITOCHONDRIAL ENCEPHALOMYOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES; ** NASH = NON-ALCOHOLIC STEATOHEPATITIS; *** SARS = SEVERE ACUTE RESPIRATORY SYNDROME

ESTIMATES AS OF 11 JANUARY 2024 SOURCE: VALUATIONLAB ESTIMATES, THIOGENESIS THERAPEUTICS

In Europe, Thiogenesis has identified MELAS and Rett syndrome as the first potential targets for clinical development of TTI-0102. The company intends to file an Investigational

Medicinal Product Dossier (IMPD) with the EMA to conduct phase II POC clinical trials in MELAS and in Rett syndrome. In the US, Thiogenesis plans to file an Investigation New Drug (IND) application in pediatric NASH, which would be a phase II POC clinical trial if accepted by the FDA.

MELAS (orphan indication) – First orphan indication to start POC trial in Europe
Mitochondrial dysfunction and resulting oxidative stress are thought to be at the core of many metabolic and cellular disorders. Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) is the most prevalent of the family of mitochondrial diseases. Mitochondria are the parts of most cells responsible for making chemical energy. Many different transfer RNA (tRNA) mutations can cause MELAS. MELAS involves the buildup of lactic acid in the body, known as lactic acidosis. Symptoms include muscle weakness, headaches, seizures, vomiting, loss of appetite, and stroke-like episodes. Patients are generally identified in childhood and before the age of 20. The prevalence is over 25,000 patients in Europe and is qualified as an orphan indication. There are no approved therapies for MELAS in Europe.

Key mechanisms of action in MELAS

- Anti-oxidant, precursor to glutathione.
- Cytoprotective, precursor to taurine.
- Maintains the thiol/disulfide balance, restores the healthy oxidative status in the mitochondria.

TTI-0102 has multiple mechanisms of action that have the potential as a therapeutic for MELAS. It is a precursor to the important antioxidant glutathione, which reduces oxidative stress in the mitochondria. It also crosses the blood-brain barrier (BBB) and is a precursor to hypo-taurine, which oxidizes into the amino acid taurine. Taurine is well known to reduce seizures.

Rett syndrome (orphan indication) – 2nd orphan indication to start POC trial in Europe
Rett syndrome is a neurological disorder that affects young girls and is caused by mutations in the MECP2 gene that are critical in the development of the brain. Its symptoms include slowed growth, loss of motor skills, loss of communication abilities, intellectual disability, difficulty breathing, and sleep apnea, but its most identifiable symptoms are rapid hand movements and seizures. A key trait in Rett syndrome patients is the down regulation of Brain Derived Neurotropic Factor (BDNF). BDNF is a protein that creates nerve cells, aids in their survival, and creates synapses important in the connections and communications between cells. The prevalence is 1 in 10,000 girls, with an estimated 27,000 girls with Rett syndrome in Europe, and there are no approved therapies. It is considered an orphan disease by the European Medicines Agency (EMA). TTI-0102 was granted the orphan medicine designation for Rett syndrome by the EMA in 2021, providing 10-year orphan disease market exclusivity.

Key mechanisms of action in Rett syndrome

- Promotes the increase of BDNF
- Maintains the thiol/disulfide balance and healthy oxidative status in the mitochondria
- Anti-oxidant, precursor to glutathione
- Cytoprotective, precursor to taurine

TTI-0102 has two key mechanisms of action that have the potential to become a therapy for Rett syndrome. The first is that it promotes Brain Derived Neurotropic Factor (BDNF), which is beneficial for neurological disorders because it plays an important role in developing the health of neurons and synapses and maintaining the health of the brain. Second, recent studies have shown that oxidative stress in the mitochondria is an important contributor to Rett syndrome. TTI-0102, as a precursor to the antioxidant glutathione, helps combat oxidative stress and restore healthy mitochondrial function.

Pediatric NASH (large indication) – First large indication with POC to start in the US
Nonalcoholic fatty liver disease (NAFLD) is a condition in which excess fat builds up in the liver. If left untreated, NAFLD often progresses to nonalcoholic steatohepatitis (NASH), which results in pronounced liver inflammation, irreversible liver damage, and fibrosis. Historically, NASH was mostly observed in adult patients, but with the worldwide increase in childhood obesity, there has been a significant escalation of NAFLD in up to 7 mn children and more than 1.5 mn children with NASH, in the US alone. Pediatric NASH can lead to severe and irreversible liver disease in children, resulting in cirrhosis (permanent scarring), liver failure, and liver cancer with the need for transplant. There are currently no drugs approved for NASH in the US, with a far lower activity in clinical trials for pediatric NASH.

Key mechanisms of action in NASH

- Anti-oxidant, precursor to glutathione
- Anti-inflammatory
- Maintains the thiol/disulfide balance, restores the healthy oxidative status in the mitochondria

Pediatric NASH is considered a metabolic disease, many of which have now been studied for signs of oxidative stress in the mitochondria. Recent publications have shown that a functional, healthy mitochondria is an important feature of healthy liver function. TTI-0102's most significant mechanism of action is as a precursor to one of the most important antioxidants, glutathione. Increased rates of glutathione have shown potential in reducing inflammation and fibrosis in pediatric NASH patients in previous clinical trials.

In the following section, we provide an in-depth analysis of Thiogenesis' key driver TTI-0102 in:

- **MELAS** (page 20)
- **Rett syndrome** (page 25)
- **Pediatric NASH** (page 29)

Forecasts & Sensitivity Analysis

TTI-0102 in MELAS (orphan indication)

Product Analysis

MELAS peak sales of CAD 4 bn (USD 2.9 bn)- rNPV of CAD 5.5 per share

We forecast peak sales of CAD 4 bn (USD 2.9 bn) for TTI-0102 in MELAS, assuming first market launches in 2027, orphan drug and pediatric market exclusivity until 2038 (EU: 12 years), and patent expiry in 2037 (North America), an annual treatment cost per patient of between USD 350,000 (US) and EUR 200,000 (EU), and a market penetration peaking at ~50% of eligible diagnosed MELAS patients. Accounting for M&S costs (paid to contract sales organizations - CSOs) and COGS (~10% of product sales), and approximately CAD 10 mn R&D costs, our risk-adjusted NPV amounts to CAD 311 mn or CAD 5.5 per share with a conservative 5% (phase II-ready) success probability, and a WACC of 13% (consisting of a risk-free rate of 4% and a specific risk of 9%).

Note: our success rate will increase to 15% upon the start of the POC trial in Q1 2024.

MELAS – The first and most prevalent mitochondrial disease targeted by TTI-1012

MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) is the first and most prevalent mitochondrial disease targeted by TTI-0102, with an estimated ~17,000 patients in North America (US and Canada) and ~27,000 patients in Europe (excluding CEE countries), with no approved treatments. Mitochondrial diseases typically are long-term, genetic, and often-inherited disorders. MELAS is the most prevalent mitochondrial disease, affecting ~23% of patients, and is considered an orphan (rare) disease in the US and EU. MELAS is a rare, progressive genetic disorder of the mitochondria (organelles in a cell that generate its energy or the powerhouse of the cell) caused by a mutation in mitochondrial DNA that affects the nervous system and muscles. Problems with the nervous system and muscles, lactic acidosis (build-up of lactic acid in the blood), and stroke-like episodes are identifiers of the condition. MELAS normally manifests between the ages of 2 and 15 years of age, with 75% of cases diagnosed before the age of 20. Seizures, recurrent headaches, difficulty understanding or thinking, hallucinations, temporary muscle weakness or paralysis, loss of appetite, and vomiting are the most commonly reported symptoms, correlating with the side effects of lactic acidosis. Survival is around 17 years following the onset of seizures or other nervous system symptoms. The genetic disorder is passed on from mother to child, while MELAS-affected males are unable to pass on the mutation.

Broad range in prevalence rates likely caused by differences in awareness and testing

According to GlobalData, western markets have the highest diagnosed prevalence rates, with a rate of 0.00095% seen in the US, UK, Spain, Italy, Germany, France, Australia, and Canada. Brazil, India, Mexico, Russia, and South Africa have a slightly lower diagnosed prevalence rate of 0.00057%. The Asian markets of China, South Korea, and Japan have the lowest figure, with a rate of 0.00018%. More data is needed to predict future trends worldwide accurately. There is no significant evidence to suggest MELAS is associated with ethnicity, and as such, the cause for higher rates being seen in the Western markets may be due to more awareness of the disease resulting in more frequent and accurate testing.

Treatment limited to symptomatic treatment, nutritional support and coenzyme Q10
There is no specific treatment for MELAS. Current treatment is limited to managing symptoms and improving quality of life. The approach to managing MELAS typically involves a multidisciplinary team of healthcare professionals focused on **symptomatic treatment** (drugs for seizures or lactic acidosis while physical, occupational and speech therapy can help address motor and development issues); **nutritional support** (a well-balanced diet and supplements to support overall health and energy metabolism); **coenzyme Q10 supplementation** (CoQ10 plays a role in energy production with cells, CoQ10 supplements may be prescribed although the evidence on its effectiveness is limited and varies among individuals); and **lifestyle modifications** (avoidance of triggers such as illness, stress, or certain medications).

TTI-0102 improves mitochondrial function through several mechanisms of action
The key mechanisms of action for TTI-0102 applied to MELAS are its thiol-disulfide balancing mechanism (redox activity) and acting as a precursor to glutathione (powerful antioxidant) and taurine (cytoprotective). TTI–0102, as a prodrug of cysteamine, can potentially contribute to improved mitochondrial function through several mechanisms of action. Cysteamine's mechanisms of action that could play a role in treating mitochondrial disease include:

- **Restores damaged mitochondria cells:** due to certain known chemical interactions, cysteamine restores damaged mitochondria cells in the body to allow them to function normally.
- **Precursor to taurine:** cysteamine is a precursor to the amino acid taurine, which has cytoprotective properties; MELAS is often associated with taurine deficiency (Schaffer et al., 2017).
- **Precursor to glutathione**: cysteamine is a precursor to glutathione and helps to maintain glutathione levels, one of the most powerful antioxidants in the body (Enns et al., 2018)**.**
- **Coenzyme A synthesis:** cysteamine also helps contribute to the synthesis of Coenzyme A, which is necessary to produce fatty acids and contributes to the health of cell membranes (Gallego-Villar et al., 2017).

Preliminary evidence that cysteamine has a therapeutic benefit in MELAS
There is preliminary clinical evidence that cysteamine has a therapeutic benefit in humans with MELAS. There have been small clinical trials and case reports in Europe where cysteamine was successfully used in MELAS patients, although these were not controlled clinical trials required for regulatory approval. There has also been a small study by clinical centers of excellence in mitochondrial diseases (Stanford, Akron, Houston, etc.) where MELAS patients (n=25) were given Procysbi (delayed-release cysteamine), but data has yet to be published.

MELAS POC trial to start in Q1 2024 in EU, completion one year later (Q1 2025)
In October 2023, Thiogenesis filed its European Investigational Medicinal Product Dossier (IMPD) application for a phase II proof-of-concept (POC) trial with TTI-0102 for the treatment of MELAS to be conducted in France and the Netherlands. The company plans to start a phase IIa proof-of-concept (POC) trial in Q1 2024 using the powder formulation of TTI-0102 that was used in the previous safety trial. Trial completion is expected roughly 1 year later (Q1 2025), with topline results to report shortly after. The primary endpoint is improvement in a 12-minute walk test (12MWT), with secondary endpoints yet to be determined. An

interim (futility) analysis is planned for 6-9 months (H2 2024) after the start of the trial. The POC trial is expected to cost approximately CAD 5 mn.

Upon positive POC results, the company plans to file for approval in the EU based on the hybrid MAA (marketing authorization application) regulatory pathway. This pathway is available when a manufacturer develops a medicine that is based on a reference medicine (in this case, cysteamine) but has a different strength or a different route of administration (TTI-0102 is a prodrug of cysteamine with a naturally controlled release administration compared to (immediate-release) cysteamine with spikes) or a different indication from the reference medicine (TTI-0102 targets MELAS instead of cystinosis). In the US, the FDA filing will be based on the 505(b)(2) regulatory pathway, similar to the EU hybrid MAA, with cysteamine as the reference drug. This saves substantial time and development costs as much of the required safety data for TTI-0102 can be referenced to cysteamine in previous clinical trials. First sales in the EU and US are expected in 2027. The company plans to apply for early access programs (EAPs) in the EU and the US, which could generate initial, albeit minor (single-digit million Canadian dollars) revenues in 2026.

MELAS (orphan indication) peak sales potential of CAD 4 bn (USD 2.9 bn)

The estimated prevalence of MELAS ranges widely from 1 to 16 per 100,000 people in the population as is often the case with rare diseases with no effective treatments. We estimate there are ~17,000 MELAS patients in North America (US and Canada) and ~27,000 patients in Europe (excluding the Central Eastern European (CEE) countries). We have conservatively excluded other regions due to the lack of clinical diagnosis and affordability of relatively expensive orphan drug treatments.

To be conservative, we assume only 10% of MELAS patients are diagnosed, and 80% of patients are eligible for TTI-0102 treatment. There is a low rate of diagnosis and a high rate of misdiagnosis as the disease manifests with a wide range of symptoms affecting multiple organ systems, including neurological, muscular, and metabolic systems, while the onset and progression of MELAS symptoms can vary widely among individuals. Moreover, some MELAS symptoms, such as seizures, stroke-like episodes, and muscle weakness, can resemble those of other neurological or metabolic disorders. If TTI-0102 or other treatments are approved for MELAS, awareness of the disease and genetic testing often required for a definitive diagnosis are expected to increase, leading to a substantially higher diagnosis rate. We expect the assumed low 10% diagnosis rate to increase to approximately 50% in 5-7 years after the launch of TTI-0102.

The first launches of TTI-0102 in MELAS are expected in 2027. Thiogenesis plans to commercialize TTI-0102 in MELAS and other orphan indications such as Rett syndrome through regional or local contract sales organizations (CSOs) to maximize long-term profitability. Consequently, Thiogenesis will book product revenues and incur COGS (we assume 10% of product sales) and M&S costs (paid to the CSOs) with approximately CAD 10 mn remaining R&D costs up to approval.

In our detailed MELAS forecasts, we have conservatively accounted for two major regions, namely:

1) **North America (US & Canada):** peak sales are expected to amount to CAD 2.1 bn (USD 1.5 bn), assuming an annual treatment cost per patient of USD 350,000 (CAD 472,778), patent protection until 2037 (excluding potential patent term extensions), and a ~50% peak penetration rate reflecting the high unmet medical need.

2) **Europe (excl. CEE countries):** we forecast peak sales to amount to CAD 2 bn (USD 1.5 bn), assuming an annual treatment cost per patient of EUR 200,000 (CAD 291,288), orphan and pediatric market exclusivity until 2039 and a peak market penetration rate of ~45%, reflecting the high unmet medical need.

We calculate a risk-adjusted (r)NPV for TTI-0102 in MELAS of CAD 311 mn or CAD 5.5 per share based on a conservative 5% (phase II-ready) historical success rate and a WACC of 13% consisting of a risk-free rate (10-year Canadian bond yield) of 4%, and a specific risk of 9%, based on a market risk premium of 6% multiplied by a beta of 1.5.

Our detailed forecasts and sensitivity analysis can be seen on the following page.

MELAS (orphan indication)

TTI-0102 - FINANCIAL FORECASTS FOR MELAS (ORPHAN INDICATION)

INDICATION	TREATMENT OF MELAS (MITOCHONDRIAL ENCEPHALOMYOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES)
DOSAGE	ONCE-DAILY ORAL PILL (DOSAGE TO BE DETERMINED)
PRICE	ANNUAL TREATMENT COST PER PATIENT - US: USD 350,000; EU: EUR 200,000
STANDARD OF CARE	NO SPECIFIC TREATMENTS; TREATMENT LIMITED TO SYMPTOMATIC TREATMENT (SEIZURES, LACTIC ACIDOSIS), NUTRITIONAL SUPPORT, COENZYME Q10 SUPPLEMENTATION
UNIQUE SELLING POINT	FIRST EFFECTIVE AND SAFE TREATMENT FOR MELAS WITH THE POTENTIAL TO IMPROVE MOBILITY

7Ps ANALYSIS

PATENT	COMPOSITION OF MATTER PATENT EXPIRES 2037 (EXCLUDING PATENT TERM EXTENSIONS); POTENTIAL ORPHAN & PEDIATRIC MARKET EXCLUSIVITY US (7.5-YEAR), EU (12-YEA
PHASE	START EU PHASE II TRIAL IN FRANCE/THE NETHERLANDS IN Q1 2024; TRIAL COMPLETION ~1 YEAR LATER (INTERIM ANALYSIS 6-9 MONTHS AFTER START)
PATHWAY	ORPHAN DRUG INDICATION - SINGLE PIVOTAL PHASE II TRIAL LIKELY SUFFICIENT FOR ACCELERATED/CONDITIONAL APPROVAL; 505(B)(2) & HYBRID MAA REGULATORY PATHWA
PATIENT	POTENTIAL TO MAINTAIN OR IMPROVE MOBILITY OR MOTOR FUNCTIONS IMPROVING THE QUALITY OF LIFE FOR PATIENTS
PHYSICIAN	FIRST SAFE AND EFFECTIVE TREATMENT WITH POTENTIAL TO IMPROVE OR MAINTAION MOBILITY AND MOTOR FUNCTIONS
PAYER	LESS OVERALL TREATMENT COSTS DUE TO THE IMPROVEMENT MOBILITY AND MOTOR SKILLS LEADING TO LESS TREATMENT IN HOSPITALS OR SPECIALIST CARE CENTERS
PARTNER	UPON APPROVAL SEEK (REGIONAL) CONTRACT SALES ORGANIZATIONS TO COMMERCIALIZE TTI-0102 IN ORPHAN INDICATIONS TO MAXIMIZE LONG-TERM PROFITABILITY

REVENUE MODEL

NORTH AMERICA (US & CANADA) - CONTRACT SALES ORGANIZATION	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS	17'004	17'344	17'691	18'045	18'406	18'774	19'149	19'532	19'923	20'322	20'728
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ELIGIBLE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE MELAS PATIENTS	13'603	13'875	14'153	14'436	14'725	15'019	15'320	15'626	15'938	16'257	16'582
PERCENTAGE DIAGNOSED (%)	10%	10%	10%	10%	10%	20%	30%	38%	44%	48%	50%
ELIGIBLE DIAGNOSED MELAS PATIENTS	1'360	1'388	1'415	1'444	1'472	3'004	4'596	5'938	7'013	7'803	8'291
PENETRATION (%)	0%	0%	0%	0%	2%	16%	28%	38%	46%	48%	49%
NUMBER OF TREATED PATIENTS	0	0	0	0	29	481	1'287	2'256	3'226	3'746	4'063
COST OF THERAPY PER YEAR (CAD)	474'515	475'718	475'718	475'718	475'718	475'718	475'718	475'718	475'718	475'718	475'718
SALES (CAD MN) - BOOKED BY THIOGENESIS	**0**	**0**	**0**	**0**	**14**	**229**	**612**	**1'073**	**1'535**	**1'782**	**1'933**
CHANGE (%)						1532%	168%	75%	43%	16%	8%
COGS (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
COGS (CAD MN)	0	0	0	0	-1	-23	-61	-107	-153	-178	-193
R&D COSTS (CAD MN)	0	0	0	-4	0	0	0	0	0	0	0
M&S COSTS (CAD MN)	0	0	0	-7	-20	-34	-45	-53	-53	-53	-53
PROFIT BEFORE TAX (CAD MN)	**0**	**0**	**0**	**-11**	**-8**	**172**	**506**	**913**	**1'328**	**1'551**	**1'686**
TAX RATE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
TAXES (CAD MN)	0	0	0	1	1	-20	-58	-105	-153	-178	-194
PROFIT (CAD MN)	**0**	**0**	**0**	**-10**	**-7**	**152**	**448**	**808**	**1'175**	**1'372**	**1'492**

EUROPE (EXCL. CEE COUNTRIES) - CONTRACT SALES ORGANIZATION	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS	27'937	28'496	29'066	29'647	30'240	30'845	31'462	32'091	32'733	33'388	34'056
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ELIGIBLE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE MELAS PATIENTS	22'350	22'797	23'253	23'718	24'192	24'676	25'170	25'673	26'187	26'710	27'245
PERCENTAGE DIAGNOSED (%)	10%	10%	10%	10%	10%	15%	25%	33%	39%	43%	47%
ELIGIBLE DIAGNOSED MELAS PATIENTS	2'235	2'280	2'325	2'372	2'419	3'701	6'292	8'472	10'213	11'485	12'805
PENETRATION (%)	0%	0%	0%	0%	4%	13%	23%	31%	37%	41%	43%
NUMBER OF TREATED PATIENTS	0	0	0	9	97	481	1'447	2'626	3'779	4'709	5'506
COST OF THERAPY PER YEAR (CAD)	293'809	292'723	292'723	292'723	292'723	292'723	292'723	292'723	292'723	292'723	292'723
SALES (CAD MN) - BOOKED BY THIOGENESIS	**0**	**0**	**0**	**3**	**28**	**141**	**424**	**769**	**1'106**	**1'378**	**1'612**
CHANGE (%)					920%	397%	201%	81%	44%	25%	17%
COGS (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
COGS (CAD MN)	0	0	0	0	-3	-14	-42	-77	-111	-138	-161
R&D COSTS (CAD MN)	-1	-3	-1	-1	0	0	0	0	0	0	0
M&S COSTS (CAD MN)	0	0	0	0	-15	-29	-44	-56	-67	-67	-67
PROFIT BEFORE TAX (CAD MN)	**-1**	**-3**	**-1**	**2**	**11**	**97**	**337**	**636**	**928**	**1'173**	**1'383**
TAXES (CAD MN)	0	0	0	0	-1	-11	-39	-73	-107	-135	-159
PROFIT (CAD MN)	**-1**	**-2**	**-1**	**2**	**10**	**86**	**299**	**563**	**821**	**1'038**	**1'224**

	2023E	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
GLOBAL SALES (CAD MN)	**0**	**0**	**0**	**3**	**42**	**369**	**1'036**	**1'842**	**2'641**	**3'160**	**3'544**
CHANGE (%)					1424%	773%	180%	78%	43%	20%	12%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**2**	**31**	**272**	**762**	**1'355**	**1'943**	**2'325**	**2'608**
GLOBAL PROFIT (CAD MN)	**-1**	**-2**	**-1**	**-8**	**3**	**238**	**746**	**1'371**	**1'997**	**2'411**	**2'717**
CHANGE (%)		69%	-59%	795%	-134%	8647%	213%	84%	46%	21%	13%

WACC (%)	13%	
NPV TOTAL PROFIT (CAD MN)	**6'224**	
NUMBER OF SHARES (MN)	56.9	
NPV PER SHARE (CAD)	109	
SUCCESS PROBABILITY	5%	(PHASE II-READY)
RISK ADJUSTED NPV PER SHARE (CAD)	**5.5**	

SENSITIVITY ANALYSIS

		WACC (%)				
	CAD/SHARE	11	12	13	14	15
	100%	131.0	119.3	109.4	99.3	90.8
	80%	104.8	95.4	87.5	79.4	72.6
	65%	85.1	77.5	71.1	64.5	59.0
SUCCESS PROBABILITY	50%	65.5	59.6	54.7	49.7	45.4
	35%	45.8	41.7	38.3	34.8	31.8
	15%	19.6	17.9	16.4	14.9	13.6
	5%	6.5	6.0	**5.5**	5.0	4.5

ESTIMATES AS OF 11 JANUARY 2024

SOURCE: VALUATIONLAB ESTIMATES

TTI-0102 in Rett syndrome (orphan indication)

Product Analysis

Rett syndrome peak sales of CAD 1.5 bn (USD 1.1 bn)- rNPV of CAD 2.5 per share

We forecast peak sales of CAD 1.5 bn (USD 1.1 bn) for TTI-0102 in Rett syndrome, assuming first market launches in late 2026 (EU), orphan drug and pediatric market exclusivity providing protection until 2038 (Europe) and patent expiry in 2037 (North America), an annual treatment cost per patient of between USD 350,000 (North America) and EUR 200,000 (Europe), and a market penetration peaking at ~50% of eligible diagnosed Rett syndrome patients. Accounting for M&S costs (paid to contract sales organizations - CSOs) and COGS (~10% of product sales), and approximately CAD 2 mn R&D costs, our risk-adjusted NPV amounts to CAD 140 mn or CAD 2.5 per share with a conservative success probability of 5% (phase II-ready), and a WACC of 13%.

Note: Our success rate will increase to 15% upon the start of the POC trial in mid-2024.

Rett syndrome – a severe neuro-development disorder affecting young girls

Rett syndrome is a rare but severe neuro-development disorder primarily affecting females from infancy, with approximately 17,000 patients in North America and ~25,000 in the EU, with an incidence of 1 out of 10,000 to 15,000 live female births. Rett syndrome is a genetic disease caused by abnormalities in the MECP2 (methyl CpG-binding protein 2) gene, which has important information for the normal functioning of nerve cells and is critical in the development of the brain. The MECP2 gene is in the X chromosome, one of the two sex chromosomes (X and Y) that determine gender. Rett syndrome almost exclusively affects girls (XX). Boys (XY) have only one X chromosome, and if affected, they usually do not survive until birth. Although the disease is genetic, most girls affected (over 95%) do not inherit it from their parents. Patients develop normally until 6-18 months of life when there is a slowing down or stagnation of skills that include loss of fine motor skills and speech, stereotypic abnormal hand movements, severe digestive problems, irregular heartbeat, seizures, and disordered breathing such as sudden and frequent breath holds (apnea). It is estimated that 20-26% of deaths in girls with Rett syndrome are attributed to sudden and severe cardiorespiratory dysregulation (disordered breathing that leads to irregular and often fatal heartbeats and sudden death). Rett syndrome patients are considered to be on the autistic spectrum.

Treatment is limited to symptomatic treatment, physical and occupational therapy

There is no specific cure for Rett syndrome. Current treatment is limited to the management of symptoms and improving quality of life. The approach to managing Rett syndrome typically involves a multidisciplinary team of healthcare professionals focused on **symptomatic treatment** (to manage and alleviate specific symptoms such as motor difficulties, seizures, breathing irregularities, sleep disturbances, or anxiety); **physical and occupational therapy** (to maintain or improve motor skills, coordination, and activities of daily living); **communication aids** (such as picture boards or assistive communication devices); and **behavioral and psychological interventions** (to help manage behavioral challenges and improve overall well-being).

TTI-0101 has three key mechanisms of action in Rett syndrome

TTI–0102 is believed to have three key mechanisms of action for the potential treatment of Rett syndrome that promote neuronal survival and growth, have positive effects on the mitochondria and may help overcome the effects of the genetic mutation. These include:

1) **Promotion of BDNF:** cysteamine promotes the production of brain-derived neurotropic factor (BDNF), which is typically deficient in Rett syndrome patients and is important in neuronal survival and growth, in addition to having antioxidant properties and positive effects on the mitochondria. A French academic group has done significant research into the therapeutic benefits of increasing BDNF for Rett syndrome and Huntington's disease. Importantly, they have observed the huntingtin protein that is mutated in Huntington's disease may be related to the development of Rett syndrome as well (Roux et al., 2012). The huntingtin protein is important because it is involved in the transport of BDNF. In addition to compelling animal studies by academics, Raptor Pharmaceuticals (now Amgen) has previously completed a promising, but not decisive, trial using Procysbi (delayed-release cysteamine) to treat Huntington's disease patients based on increasing BDNF levels.

2) **Missense mutation:** another mechanism of action that could be beneficial in treating Rett syndrome is that the TTI–0102 generated cysteamine - in a naturally controlled manner - may help overcome the effects of a genetic mutation caused by the disruptive replacement of arginine by cysteine in proteins, called a missense mutation, which is also a common feature in Rett syndrome *(Gallego-Villar et al., 2017).*

3) **Oxidative stress:** several studies have shown that oxidative stress plays a role in the pathogenesis of Rett syndrome. Oxidative stress is the condition where the natural balance between the production of reactive oxygen species and the antioxidant defense system is disrupted, which can cause damage to cellular components such as DNA, proteins, and lipids, leading to cellular dysfunction and death. Oxidative stress markers such as non-protein-bound iron (NPBI) and F2-isoprostanes are elevated in Rett syndrome patients. These markers indicate increased lipid peroxidation, which can impair the structure and function of cell membranes. Moreover, these markers correlate with the severity of clinical symptoms and the type of MeCP2 mutation in Rett syndrome patients (*Shulyakova et al., 2017*).

EU ODD provides 10-year market exclusivity with the potential of 2-year pediatric

In 2019, Thiogenesis received an Orphan Drug Designation (ODD) from the EMA for TTI-0102 in treating Rett syndrome. ODD provides next to unrestricted protocol assistance at reduced fees and other benefits, importantly, 10-year market exclusivity for TTI-0102 starting on the date of approval for Rett syndrome in the EU. ODD could also facilitate research grants from the European Commission or individual member states. As Rett syndrome is a pediatric disease, an additional 2-year pediatric market exclusivity period may apply for TTI-0102 as well.

Rett syndrome POC trial start mid-2024 in EU, completion ~18 months later (end 2025)

Thiogenesis expects to complete and submit an Investigational Medicinal Product Dossier (IMPD) for a phase II/III POC trial of TTI-0102 in Rett syndrome, to be conducted in a leading academic hospital in France. The trial is expected to start in mid-2024 using a new tablet formulation of TTI-0102, with trial completion approximately 18 months later (end 2025) and

topline results to report shortly after that. The primary endpoint will be the improvement of behavioral disorders as measured by the Aberrant Behavioral Checklist (ABC) scale. The POC trial is expected to cost approximately CAD 3 mn. The company plans to apply for early access programs (EAPs) in the EU and, subsequently, the US, which could generate early but small revenues in 2025.

Upon positive POC results, the company plans to file for approval in the EU using the hybrid MAA regulatory pathway and, in the US, using the 505(b)(2) regulatory pathway, which cuts timelines and costs substantially. First sales in the EU are expected in late 2026.

Rett syndrome (orphan indication) peak sales potential of CAD 1.5 bn (USD 1.1 bn)
The estimated number of Rett syndrome patients is similar to the number of MELAS patients, with an estimated ~17,000 in North America (US and Canada) and ~27,000 in Europe (excluding the CEE countries). We have conservatively excluded other regions due to the lack of clinical diagnosis and affordability of relatively expensive orphan drug treatments.

Rett syndrome is challenging to diagnose primarily because its symptoms may not manifest until the child is a few months old, and the early signs, such as developmental delays, are common in many neurodevelopmental disorders, making it hard to distinguish. Genetic testing to identify mutations in the MECP2 gene associated with Rett syndrome is a key component of diagnosis but may not always provide definite answers. It is estimated that around 10% of patients in the US are currently diagnosed. An educational effort to increase awareness of Rett syndrome among physicians and parents will be crucial to achieving our sales forecasts. We have accounted for increased diagnosis in our forecasts with diagnosed patients starting at 10% and conservatively increasing to around 20% at peak. We assume 80% of patients to be eligible for treatment.

The first launches of TTI-0102 in Rett syndrome are expected in late 2026 in Europe and in 2027 in North America. Like MELAS, Thiogenesis plans to commercialize TTI-0102 in Rett syndrome through regional and local contract sales organizations (CSOs) to maximize long-term profitability. Thiogenesis will book product revenues and incur COGS (we assume 10% of product sales) and M&S costs (paid to the CSOs) with approximately CAD 2 mn remaining R&D costs up to approval.

In our detailed Rett syndrome forecasts, we have conservatively accounted for two major regions, namely:

1) **North America (US & Canada):** peak sales are expected to amount to CAD 800 mn (USD 600 mn), assuming an annual treatment cost per patient of USD 350,000 (CAD 472,778), patent protection until 2037 (excluding potential patent term extensions), and a ~50% peak penetration rate reflecting the high unmet medical need.
2) **Europe (excl. CEE countries):** we forecast peak sales to amount to CAD 800 mn (USD 600 mn), assuming an annual treatment cost per patient of EUR 200,000 (CAD 291,288), orphan and pediatric market exclusivity until 2038 and a peak market penetration rate of ~45%, reflecting the high unmet medical need.

We calculate a rNPV for TTI-0102 in Rett syndrome of CAD 140 mn or CAD 2.5 per share based on a conservative 5% (phase II-ready) historical success rate and a WACC of 13%.

Our detailed forecasts and sensitivity analysis can be seen on the following page.

Rett syndrome (orphan indication)

TTI-0102 - FINANCIAL FORECASTS FOR RETT SYNDROME (ORPHAN INDICATION)

INDICATION	TREATMENT OF RETT SYNDROME
DOSAGE	ONCE-DAILY ORAL PILL (DOSAGE TO BE DETERMINED)
PRICE	ANNUAL TREATMENT COST PER PATIENT - US: USD 350,000; EU: EUR 200,000
STANDARD OF CARE	NO SPECIFIC TREATMENT FOR RETT SYNDROME; TREATMENT LIMITED TO SYMPTOMATIC TREATMENT, PHYSICAL AND OCCUPATIONAL THERAPY
UNIQUE SELLING POINT	POTENTIALLY FIRST SAFE AND EFFECTIVE TREATMENT WITH THE POTENTIAL TO IMPROVE BEHAVIORAL DISORDERS

7Ps ANALYSIS

PATENT	COMPOSITION OF MATTER PATENT EXPIRES 2037 (EXCLUDING PATENT TERM EXTENSIONS); POTENTIAL ORPHAN & PEDIATRIC MARKET EXCLUSIVITY US (7.5-YEAR), EU (12-YE
PHASE	START EU PHASE II/III TRIAL IN FRANCE IN MID-2024, TOPLINE RESULTS AROUND 18 MONTHS LATER (INTERIM ANALYSIS 6-9 MONTHS AFTER START)
PATHWAY	ORPHAN DRUG INDICATION - SINGLE PIVOTAL PHASE II TRIAL LIKELY SUFFICIENT FOR ACCELERATED/CONDITIONAL APPROVAL; 505(B)(2) & HYBRID MAA REGULATORY PATHW
PATIENT	POTENTIAL TO MAINTAIN OR IMPROVE BEHAVIORAL DISORDERS IMPROVING THE QUALITY OF LIFE OF PATIENTS AND PARENTS
PHYSICIAN	FIRST SAFE AND EFFECTIVE TREATMENT WITH POTENTIAL DISEASE MODIFYING FEATURES
PAYER	LESS OVERALL TREATMENT COSTS DUE TO THE IMPROVEMENT OF BEHAVIORAL SKILLS LEADING TO LESS TREATMENT IN HOSPITALS OR SPECIALIST CARE CENTERS
PARTNER	UPON APPROVAL SEEK (REGIONAL) CONTRACT SALES ORGANIZATIONS TO COMMERCIALIZE TTI-0102 IN ORPHAN INDICATIONS TO MAXIMIZE LONG-TERM PROFITABILITY

REVENUE MODEL

NORTH AMERICA (US & CANADA) - CONTRACT SALES ORGANIZATION	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS	17'004	17'344	17'691	18'045	18'406	18'774	19'149	19'532	19'923	20'322	20'728
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ELIGIBLE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE RETT SYNDROME PATIENTS	13'603	13'875	14'153	14'436	14'725	15'019	15'320	15'626	15'938	16'257	16'582
PERCENTAGE DIAGNOSED (%)	10%	10%	10%	10%	15%	17%	18%	19%	19%	20%	20%
ELIGIBLE DIAGNOSED RETT SYNDROME PATIENTS	1'360	1'388	1'415	1'444	2'209	2'553	2'758	2'891	3'028	3'170	3'316
PENETRATION (%)	0%	0%	0%	0%	4%	16%	28%	38%	46%	48%	49%
NUMBER OF TREATED PATIENTS	0	0	0	0	88	409	772	1'099	1'393	1'522	1'625
COST OF THERAPY PER YEAR (CAD)	474'515	475'718	475'718	475'718	475'718	475'718	475'718	475'718	475'718	475'718	475'718
SALES (CAD MN) - BOOKED BY THIOGENESIS	**0**	**0**	**0**	**0**	**42**	**194**	**367**	**523**	**663**	**724**	**773**
CHANGE (%)						362%	89%	42%	27%	9%	7%
COGS (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
COGS (CAD MN)	0	0	0	0	-4	-19	-37	-52	-66	-72	-77
R&D COSTS (CAD MN)	0	0	0	0	0	0	0	0	0	0	0
M&S COSTS (CAD MN)	0	0	0	0	-20	-34	-41	-48	-50	-45	-41
PROFIT BEFORE TAX (CAD MN)	**0**	**0**	**0**	**0**	**17**	**141**	**290**	**423**	**546**	**606**	**655**
TAX RATE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
TAXES (CAD MN)	0	0	0	0	-2	-16	-33	-49	-63	-70	-75
PROFIT (CAD MN)	**0**	**0**	**0**	**0**	**15**	**125**	**256**	**374**	**483**	**537**	**580**

EUROPE (EXCL. CEE COUNTRIES) - CONTRACT SALES ORGANIZATION	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS	27'937	28'496	29'066	29'647	30'240	30'845	31'462	32'091	32'733	33'388	34'056
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ELIGIBLE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE RETT SYNDROME PATIENTS	22'350	22'797	23'253	23'718	24'192	24'676	25'170	25'673	26'187	26'710	27'245
PERCENTAGE DIAGNOSED (%)	10%	10%	10%	15%	17%	18%	19%	19%	20%	20%	20%
ELIGIBLE DIAGNOSED RETT SYNDROME PATIENTS	2'235	2'280	2'325	3'558	4'113	4'442	4'656	4'878	5'106	5'342	5'449
PENETRATION (%)	0%	0%	0%	1%	14%	24%	32%	38%	42%	44%	45%
NUMBER OF TREATED PATIENTS	0	0	0	18	576	1'066	1'490	1'854	2'145	2'351	2'452
COST OF THERAPY PER YEAR (CAD)	293'809	292'723	292'723	292'723	292'723	292'723	292'723	292'723	292'723	292'723	292'723
SALES (CAD MN) - BOOKED BY THIOGENESIS	**0**	**0**	**0**	**5**	**169**	**312**	**436**	**543**	**628**	**688**	**718**
CHANGE (%)					3137%	85%	40%	24%	16%	10%	4%
COGS (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
COGS (CAD MN)	0	0	0	-1	-17	-31	-44	-54	-63	-69	-72
R&D COSTS (CAD MN)	0	-1	-1	0	0	0	0	0	0	0	0
M&S COSTS (CAD MN)	0	0	0	0	-22	-37	-44	-51	-54	-49	-44
PROFIT BEFORE TAX (CAD MN)	**0**	**-1**	**-1**	**5**	**130**	**244**	**349**	**437**	**511**	**571**	**602**
TAXES (CAD MN)	0	0	0	-1	-15	-28	-40	-50	-59	-66	-69
PROFIT (CAD MN)	**0**	**-1**	**-1**	**4**	**115**	**216**	**309**	**387**	**452**	**505**	**533**

	2023E	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
GLOBAL SALES (CAD MN)	**0**	**0**	**0**	**5**	**211**	**506**	**803**	**1'065**	**1'290**	**1'412**	**1'491**
CHANGE (%)					3944%	140%	59%	33%	21%	9%	6%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**4**	**155**	**373**	**591**	**784**	**949**	**1'039**	**1'097**
GLOBAL PROFIT (CAD MN)	**0**	**-1**	**-1**	**4**	**130**	**341**	**565**	**761**	**935**	**1'041**	**1'113**
CHANGE (%)			-32%	-560%	3040%	162%	66%	35%	23%	11%	7%

WACC (%)	13%	
NPV TOTAL PROFIT (CAD MN)	**2'807**	
NUMBER OF SHARES (MN)	57.2	
NPV PER SHARE (CAD)	49	
SUCCESS PROBABILITY	5%	(PHASE II-READY)
RISK ADJUSTED NPV PER SHARE (CAD)	**2.5**	

SENSITIVITY ANALYSIS

		WACC (%)				
	CAD/SHARE	11	12	13	14	15
	100%	58.2	53.5	49.2	45.3	41.8
	80%	46.6	42.8	39.3	36.2	33.4
	65%	37.8	34.8	32.0	29.4	27.2
SUCCESS PROBABILITY	50%	29.1	26.7	24.6	22.7	20.9
	35%	20.4	18.7	17.2	15.9	14.6
	15%	8.7	8.0	7.4	6.8	6.3
	5%	2.9	2.7	**2.5**	2.3	2.1

ESTIMATES AS OF 11 JANUARY 2024

SOURCE: VALUATIONLAB ESTIMATES

TTI-0102 in pediatric NASH (large indication)

Product Analysis

Pediatric NASH peak sales of CAD 4 bn (USD 3 bn)- rNPV of CAD 0.8 per share

We forecast peak sales of CAD 4 bn (USD 3 bn) for TTI-0102 in pediatric NASH, assuming the first market launches in 2030 by its global development and commercialization partner, orphan drug, and pediatric market exclusivity providing protection until 2038 (Europe) and patent expiry in 2037 (North America), an annual treatment cost per patient of between USD 30,000 (North America) and EUR 20,000 (Europe), and a market penetration peaking at ~4% (North America) and ~2% (Europe) of eligible diagnosed pediatric NASH patients. Upon positive POC trial results expected in 2025, we expect Thiogenesis to sign on with a global development and commercialization partner in 2026, with an upfront payment of CAD 49 mn and up to CAD 1.6 bn additional development, regulatory, and sales milestones, and 10% royalties on net sales. Based on the above, our risk-adjusted NPV amounts to CAD 46 mn or CAD 0.8 per share with a conservative success probability of 5% (phase II-ready), and a WACC of 13%.

Note: Our success rate will increase to 15% upon the start of the POC trial in mid-2024. We do not include forecasts for adult NASH, which could be substantial. Additional pivotal trials will be needed.

NASH is common in children largely due to the rise in childhood obesity

The first large indication for TTI-0102 is pediatric nonalcoholic steatohepatitis (NASH), a serious form of nonalcoholic fatty liver disease (NAFLD). NAFLD is a condition in which excess fat builds up in the liver, not caused by heavy alcohol use. NAFLD is the most common cause of chronic liver disease in the US and other Western countries, with an estimated 5% to 10% of children affected. NAFLD has become more common in children in recent decades, in part because of the rise in childhood obesity.

There are two types of nonalcoholic fatty liver disease:

1. **NAFL (nonalcoholic fatty liver):** the form of NAFLD in which a child has increased fat in the liver but little or no inflammation or liver damage. NAFL typically does not progress to cause liver damage or complications.
2. **NASH (nonalcoholic steatohepatitis):** the form of NAFLD in which a child has inflammation of the liver and liver damage in addition to fat in the liver, which can cause fibrosis (scarring of the liver) or cirrhosis in which the liver is scarred and permanently damaged. Cirrhosis can lead to liver cancer or liver failure with the need for a transplant.

A silent disease affecting more than 15 mn children in Western countries

Children typically develop one type of NAFLD or the other, although sometimes, children with one form are later diagnosed with the other form of NAFLD. NAFL is a mild condition, and NASH is a more serious condition. Experts are not sure why some children with NAFLD have NASH while others have NAFL. Research suggests that 20% to 50% of children with NAFLD have the NASH form of the disease. Usually, NAFLD, including NAFL and NASH, is a silent disease with few or no symptoms. Children may not have symptoms even if they develop cirrhosis due to NASH. However, once symptoms arise, a child may already have permanent liver damage. If children do have symptoms from NASH, they may feel tired, become tired easily, or have discomfort over the liver in the upper right side of the abdomen.

There are an estimated 7 mn children with pediatric NAFLD in the US alone, with an estimated 8 mn in Europe assuming a similar prevalence rate as in the US.

Main risk factors include obesity, metabolic syndrome, diabetes & unhealthy diet
Children at risk of NASH typically share common risk factors, including **obesity** (excess body weight, especially when associated with abdominal obesity, is often linked to fat accumulation in the liver); **insulin resistance** (a condition when the body's cells do not respond effectively to insulin, which often occurs with obesity, and may contribute to liver fat accumulation); **type 2 diabetes** (children with type 2 diabetes are at an elevated risk of NASH; insulin resistance is a common factor linking both conditions); **metabolic syndrome** (a cluster of conditions including obesity, high blood pressure, high blood sugar levels, and abnormal lipid (fat) levels have an increased risk of NASH); **genetic factors** (there may be a genetic predisposition to NASH and children with a family history of liver disease may be at higher risk), and; **unhealthy diet** (diets high in processed foods, sugars, and saturated fats contribute to obesity and may increase the risk of NASH).

Treatment is limited to early identification of risk factors, lifestyle modifications, and regular monitoring
There is no specific drug approved for the treatment of pediatric NASH. The early identification of risk factors, lifestyle modifications, and regular monitoring are crucial for managing and preventing the progression of NASH in children. Some general approaches include **lifestyle modifications** such as a healthy diet (well-balanced, nutritious diet low in added sugars and saturated fats) and regular exercise (physical activity is important for weight management and overall health); **weight management** (gradual and sustainable weight loss under the guidance of healthcare professionals); **monitoring and control of metabolic factors** (regular monitoring of blood sugar and lipid levels in particular if the child has insulin resistance or dyslipidemia), and; **management of coexisting conditions** (e.g., treating insulin resistance or type diabetes or high blood pressure if present).

Clinical efficacy was seen in a subset of children with NASH treated with cysteamine
There are important links between a healthy mitochondria and NASH, suggesting that potential interventions that target the thiol/disulfide balance and mitochondrial health could have a clinical benefit on NASH. In addition, there are potential benefits in treating NASH, from increasing exposure to antioxidants and anti-inflammatories like those provided by TTI-0102.

Early clinical evidence of the efficacy of cysteamine in treating pediatric NASH was seen with Raptor's (now Amgen) Procysbi, cysteamine bitartrate delayed-release formulation, in the so-called "CyNCh" trial. The results of this randomized controlled phase IIb dosing trial were published in December 2016. Twice-daily Procysbi treatment was given for 1 year in 169 children with NAFLD and a mean age of around 14 years +/- 2.7 years to evaluate if it could be an effective therapy. Although the trial missed its primary endpoint of reducing overall histologic markers of NAFLD compared to placebo, a subgroup analysis showed that in the lowest weight group (42% of the children) weighing less than 65 kg, and children younger than 13 years of age, a statistically significant histological improvement was seen. It appears that the older and heavier children were underdosed, resulting in a non-significant histological improvement for the total treatment group.

Therefore, treating children with NASH with TTI-0102, a prodrug of cysteamine that offers a naturally controlled release of cysteamine at higher doses and increased time of therapeutic exposure, has clinical promise.

A pediatric NASH POC trial is scheduled to start in the US in mid-2024

In Q2 2024, Thiogenesis expects to receive clearance for its Investigational New Drug (IND) application in pediatric NASH, allowing it to start clinical trials with TTI-0102 in the US. In mid-2024, the company expects to start a phase IIa POC trial (final trial design currently under evaluation) with TTI-0102 in children with NASH, with trial completion expected roughly 18 months later (end-2025) and report topline results shortly after. The primary endpoint will be the change percentage of hepatic steatosis (fatty liver disease) following a certain treatment period. Secondary endpoints will measure the change in several established liver biomarkers, such as aspartate aminotransferase (ALT). Upon positive POC trial results expected in 2025, Thiogenesis plans to out-license the global rights for (pediatric) NASH to a global biopharmaceutical company for further development and commercialization in return for sizeable milestone payments and royalties on sales in 2026.

Pediatric NASH (large indication) peak sales potential of CAD 4 bn (USD 3 bn)

The number of children with NAFLD is estimated to be around 7 mn in North America (US and Canada) and 8 mn in Europe (excluding the CEE countries). Roughly one-third have NASH. We assume 80% have been diagnosed, although this could be lower as many children do not have symptoms, with 90% of those diagnosed eligible for treatment with TTI-0102. The first launches in pediatric NASH are expected to start in 2030. We assume the global development and commercialization partner will pay CAD 49 mn in upfront milestones in 2026, which can be used for other potential orphan indications for TTI-0102, and up to CAD 1.6 bn in additional development, regulatory, and sales milestones next to 10% royalties on net product sales, which its partner will book. Thiogenesis is expected to incur CAD 7-10m in R&D costs to complete the POC trial.

Given the large number of patients with pediatric NASH compared to orphan indications such as MELAS and Rett syndrome, pricing should be substantially lower for pediatric NASH to receive pricing and reimbursement. Thiogenesis is expected to differentiate TTI-0102 for large and orphan indications by potentially offering different formulations with different doses and, hence, pricing.

In our detailed pediatric NASH forecasts, we have conservatively accounted for two major regions, namely:

1) **North America (US & Canada):** peak sales are expected to amount to CAD 2.8 bn (USD 2 bn), assuming an annual treatment cost per patient of USD 30,000 (CAD 40,776), patent protection until 2037 (excluding potential patent term extensions), and a conservative ~4% peak penetration rate.
2) **Europe (excl. CEE countries):** we forecast peak sales to amount to CAD 1.4 bn (USD 1.0 bn), assuming an annual treatment cost per patient of EUR 20,000 (CAD 29,272), European orphan and pediatric market exclusivity for Rett syndrome protecting the TTI-0102 franchise until 2038, and a conservative peak market penetration rate of ~2%.

We calculate an rNPV for TTI-0102 in pediatric NASH of CAD 46 mn or CAD 0.8 per share based on a conservative 5% (phase II-ready) historical success rate and a WACC of 13%. Our detailed forecasts and sensitivity analysis can be seen on the following page.

Pediatric NASH (large indication)

TTI-0102 - FINANCIAL FORECASTS FOR PEDIATRIC NASH (LARGE INDICATION)

INDICATION	TREATMENT FOR PEDIATRIC NASH (NON-ALCOHOLIC STEATOHEPATITIS)
DOSAGE	ONCE-DAILY ORAL PILL (DOSAGE TO BE DETERMINED)
PRICE	ANNUAL TREATMENT COST PER PATIENT - US: USD 30,000; EU: EUR 20,000
STANDARD OF CARE	NO SPECIFIC TREATMENTS; TREATMENT LIMITED TO EARLY IDENTIFICATION OF RISK FACTORS, LIFE STYLE MODIFICATIONS, AND REGULAR MONITORING
UNIQUE SELLING POINT	POTENTIALLY FIRST TREATMENT THAT IMPROVEs HEPATIC STEATOSIS (FATTY LIVER DISEASE) IN PEDIATRIC NASH PATIENTS

7Ps ANALYSIS

PATENT	COMPOSITION OF MATTER PATENT EXPIRES 2037 (EXCLUDING PATENT TERM EXTENSIONS); MELAS/RETT ORPHAN & PEDIATRIC DRUG EXCLUSIVITY EXTENDS PROTECTION
PHASE	START US PHASE II TRIAL IN MID-2024, TOPLINE RESULTS APPROXIMATELY 18 MONTHS LATER (INTERIM ANALYSIS 6-9 MONTHS AFTER START)
PATHWAY	LARGE INDICATION - TWO POSITIVE PIVOTAL PHASE III TRIALS WITH 1,000'S OF PATIENTS NEEDED FOR REGULATORY APPROVAL IN NORTH AMERICA AND EUROPE
PATIENT	IMPROVEMENT OF FATTY LIVER DISEASE WITH THE POTENTIAL TO REDUCE DAMAGE TO THE LIVER CAUSED BY NASH
PHYSICIAN	FIRST SAFE AND EFFECTIVE TREAMENT THAT IMPROVES FATTY LIVER DISEASE AND POTENTIAL TO REDUCE DAMAGE TO THE LIVER CAUSED BY NASH
PAYER	IMPROVEMENT OF FATTY LIVER DISEASE SHOULD LEAD TO LESS OVERALL TREATMENT COSTS SUCH AS SPECIALIST CARE OR LIVER TRANSPLANTATION
PARTNER	UPON POSITIVE POC SEEK DEVELOPMENT AND COMMERCIALIZATION PARTNER IN RETURN FOR SUBSTANTIAL UPFRONT, REGULATORY & SALES MILESTONES & SALES ROYALTIE

REVENUE MODEL

NORTH AMERICA (US & CANADA) - PARTNER	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)	6'801'668	6'937'701	7'076'455	7'217'984	7'362'344	7'509'591	7'659'783	7'812'978	7'969'238	8'128'623	8'291'195
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
CHILDREN WITH NON-ALCOHOLIC STEATOHEPATITIS (NASH) (%)	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%
CHILDREN WITH NON-ALCOHOLIC STEATOHEPATITIS (NASH)	2'266'996	2'312'336	2'358'583	2'405'754	2'453'869	2'502'947	2'553'006	2'604'066	2'656'147	2'709'270	2'763'455
PERCENTAGE DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
DIAGNOSED PEDIATRIC NASH PATIENTS	1'813'597	1'849'869	1'886'866	1'924'603	1'963'095	2'002'357	2'042'404	2'083'253	2'124'918	2'167'416	2'210'764
ELIGIBLE PATIENTS	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE DIAGNOSED PEDIATRIC NASH PATIENTS	1'632'237	1'664'882	1'698'179	1'732'143	1'766'786	1'802'122	1'838'164	1'874'927	1'912'426	1'950'674	1'989'688
PENETRATION (%)	0%	0%	0%	0%	0%	0%	0%	0.1%	1.0%	2.0%	2.8%
NUMBER OF TREATED PATIENTS	0	0	0	0	0	0	0	1'875	19'124	39'013	55'711
PATIENT COMPLIANCE (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
COST OF THERAPY PER YEAR (CAD)	40'673	40'776	40'776	40'776	40'776	40'776	40'776	40'776	40'776	40'776	40'776
SALES (CAD MN) - BOOKED BY PARTNER	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**61**	**624**	**1'273**	**1'817**
CHANGE (%)									920%	104%	43%
ROYALTY (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
ROYALTIES (CAD MN)	0	0	0	0	0	0	0	6	62	127	182
UPFRONT & MILESTONE PAYMENTS (CAD MN)	0	0	0	27	0	41	0	68	68	136	204
R&D COSTS (CAD MN)	0	-2	-4	-1	0	0	0	0	0	0	0
PROFIT BEFORE TAX (CAD MN)	**0**	**-2**	**-4**	**26**	**0**	**41**	**0**	**74**	**130**	**263**	**386**
TAX RATE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
TAXES (CAD MN)	0	0	1	-3	0	-5	0	-9	-15	-30	-44
PROFIT (CAD MN)	**0**	**-2**	**-4**	**23**	**0**	**36**	**0**	**66**	**115**	**233**	**341**

EUROPE (EXCL. CEE COUNTRIES) - PARTNER	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)	8'109'577	8'271'769	8'437'204	8'605'948	8'778'067	8'953'629	9'132'701	9'315'355	9'501'662	9'691'696	9'885'530
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
CHILDREN WITH NON-ALCOHOLIC STEATOHEPATITIS (NASH) (~33%)	2'702'922	2'756'981	2'812'120	2'868'363	2'925'730	2'984'244	3'043'929	3'104'808	3'166'904	3'230'242	3'294'847
ELIGIBLE DIAGNOSED PEDIATRIC NASH PATIENTS	1'946'104	1'985'026	2'024'727	2'065'221	2'106'525	2'148'656	2'191'629	2'235'462	2'280'171	2'325'774	2'372'290
PENETRATION (%)	0%	0%	0%	0%	0%	0%	0%	0.1%	0.9%	1.5%	1.9%
NUMBER OF TREATED PATIENTS	0	0	0	0	0	0	0	1'118	20'522	34'887	45'074
PATIENT COMPLIANCE (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
COST OF THERAPY PER YEAR (CAD)	29'381	29'272	29'272	29'272	29'272	29'272	29'272	29'272	29'272	29'272	29'272
SALES (CAD MN) - BOOKED BY PARTNER	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**26**	**481**	**817**	**1'056**
CHANGE (%)									1736%	70%	29%
ROYALTY (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
ROYALTIES (CAD MN)	0	0	0	0	0	0	0	3	48	82	106
UPFRONT & MILESTONE PAYMENTS (CAD MN)	0	0	0	22	0	29	0	51	59	73	110
R&D COSTS (CAD MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (CAD MN)	**0**	**0**	**0**	**22**	**0**	**29**	**0**	**54**	**107**	**155**	**215**
TAXES (CAD MN)	0	0	0	-3	0	-3	0	-6	-12	-18	-25
PROFIT (CAD MN)	**0**	**0**	**0**	**19**	**0**	**26**	**0**	**48**	**94**	**137**	**191**

	2023E	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
GLOBAL SALES (CAD MN)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**87**	**1'104**	**2'090**	**2'873**
CHANGE (%)									1165%	89%	37%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**64**	**813**	**1'537**	**2'114**
GLOBAL PROFIT (CAD MN)	**0**	**-2**	**-4**	**42**	**0**	**62**	**0**	**113**	**210**	**370**	**532**
CHANGE (%)			83%	-1162%	-100%		-100%		85%	76%	44%

WACC (%)	13%	
NPV TOTAL PROFIT (CAD MN)	**928**	
NUMBER OF SHARES (MN)	57.2	
NPV PER SHARE (CAD)	16	
SUCCESS PROBABILITY	5%	(PHASE II-READY)
RISK ADJUSTED NPV PER SHARE (CAD)	**0.8**	

SENSITIVITY ANALYSIS

		WACC (%)				
	CAD/SHARE	11	12	13	14	15
	100%	20.4	18.6	16.9	15.5	14.1
	80%	16.3	14.9	13.5	12.4	11.3
	65%	13.3	12.1	11.0	10.1	9.2
SUCCESS PROBABILITY	50%	10.2	9.3	8.5	7.7	7.1
	35%	7.1	6.5	5.9	5.4	4.9
	15%	3.1	2.8	2.5	2.3	2.1
	5%	1.0	0.9	**0.8**	0.8	0.7

ESTIMATES AS OF 11 JANUARY 2024

SOURCE: VALUATIONLAB ESTIMATES

Income Statement

THIOGENESIS THERAPEUTICS									SHARE PRICE (CAD)	0.75		
IFRS												
INCOME STATEMENT (CAD MN)	2022	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
PRODUCT SALES (INCLUDING PARTNERS)	**0**	**0**	**0**	**0**	**8**	**253**	**876**	**1'839**	**2'995**	**5'036**	**6'662**	**7'908**
CHANGE (%)						3068%	246%	110%	63%	68%	32%	19%
PRODUCT SALES (BOOKED BY THIOGENESIS)	**0**	**0**	**0**	**0**	**8**	**253**	**876**	**1'839**	**2'907**	**3'931**	**4'572**	**5'035**
CHANGE (%)						3068%	246%	110%	58%	35%	16%	10%
ROYALTIES	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**9**	**110**	**209**	**287**
CHANGE (%)										1165%	89%	37%
LICENSE, UPFRONT & MILESTONE INCOME	**0**	**0**	**0**	**0**	**49**	**0**	**70**	**0**	**119**	**127**	**209**	**314**
OTHER INCOME & GRANTS	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
CHANGE (%)												
REVENUES (EXCL. PARTNER SALES)	**0**	**0**	**0**	**0**	**57**	**253**	**946**	**1'839**	**3'035**	**4'168**	**4'990**	**5'636**
CHANGE (%)						343%	274%	94%	65%	37%	20%	13%
COGS	**0**	**0**	**0**	**0**	**-1**	**-25**	**-88**	**-184**	**-291**	**-393**	**-457**	**-504**
CHANGE (%)						3068%	246%	110%	58%	35%	16%	10%
AS % REVENUES					1%	10%	9%	10%	10%	9%	9%	9%
GROSS PROFIT	**0**	**0**	**0**	**0**	**56**	**228**	**858**	**1'655**	**2'745**	**3'775**	**4'533**	**5'133**
CHANGE (%)						304%	277%	93%	66%	38%	20%	13%
MARGIN					99%	90%	91%	90%	90%	91%	91%	91%
R&D	**-1**	**-1**	**-6**	**-7**	**-6**	**-5**	**-5**	**-6**	**-6**	**-6**	**-6**	**-7**
CHANGE (%)	-21%	39%	333%	1%	-3%	-21%	5%	5%	5%	5%	5%	5%
AS % REVENUES					11%	2%	1%	0%	0%	0%	0%	0%
M&S + G&A	**-1**	**-1**	**-2**	**-2**	**-11**	**-83**	**-142**	**-182**	**-216**	**-234**	**-224**	**-215**
CHANGE (%)	204%	29%	25%	20%	500%	672%	70%	28%	19%	8%	-4%	-4%
AS % REVENUES					19%	33%	15%	10%	7%	6%	4%	4%
OPERATING EXPENSES	**-2**	**-3**	**-8**	**-8**	**-18**	**-114**	**-235**	**-371**	**-513**	**-633**	**-688**	**-725**
CHANGE (%)	20%	34%	196%	5%	115%	534%	106%	58%	38%	23%	9%	5%
AS % REVENUES					31%	45%	25%	20%	17%	15%	14%	13%
EBITDA	**-2**	**-3**	**-8**	**-8**	**39**	**139**	**711**	**1'468**	**2'523**	**3'535**	**4'303**	**4'911**
CHANGE (%)	20%	34%	196%	5%	-571%	255%	411%	106%	72%	40%	22%	14%
MARGIN (%)					69%	55%	75%	80%	83%	85%	86%	87%
DEPRECIATION & AMORTIZATION	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
AS % REVENUES					0%	0%	0%	0%	0%	0%	0%	0%
EBIT	**-2**	**-3**	**-8**	**-8**	**39**	**139**	**711**	**1'468**	**2'523**	**3'535**	**4'303**	**4'911**
CHANGE (%)	20%	34%	196%	5%	-571%	255%	411%	106%	72%	40%	22%	14%
MARGIN (%)					69%	55%	75%	80%	83%	85%	86%	87%
OTHER INCOME (EXPENSES)	**-2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
PROFIT BEFORE TAXES	**-4**	**-3**	**-7**	**-8**	**40**	**140**	**712**	**1'468**	**2'523**	**3'535**	**4'303**	**4'911**
MARGIN					69%	55%	75%	80%	83%	85%	86%	87%
TAXES	**0**	**0**	**1**	**1**	**-5**	**-17**	**-83**	**-170**	**-292**	**-408**	**-497**	**-567**
TAX RATE (%)	0%	6%	10%	10%	13%	12%	12%	12%	12%	12%	12%	12%
NET PROFIT/LOSS	**-4**	**-3**	**-7**	**-7**	**35**	**122**	**628**	**1'298**	**2'231**	**3'127**	**3'806**	**4'345**
CHANGE (%)	222%	-28%	138%	5%	-590%	253%	413%	107%	72%	40%	22%	14%
MARGIN (%)					61%	48%	66%	71%	74%	75%	76%	77%
PROFIT/(LOSS) PER SHARE (IN CAD)	**-0.16**	**-0.06**	**-0.15**	**-0.16**	**0.77**	**2.73**	**14.00**	**28.91**	**49.69**	**69.65**	**84.78**	**96.76**

ESTIMATES AS OF 11 JANUARY 2024 SOURCE: VALUATIONLAB ESTIMATES

NOTE: At the end of FY 2022, Thiogenesis had a total of CAD 16 mn tax loss carryforwards, which the company can use on current and future profits.

Ratios & Balance Sheet

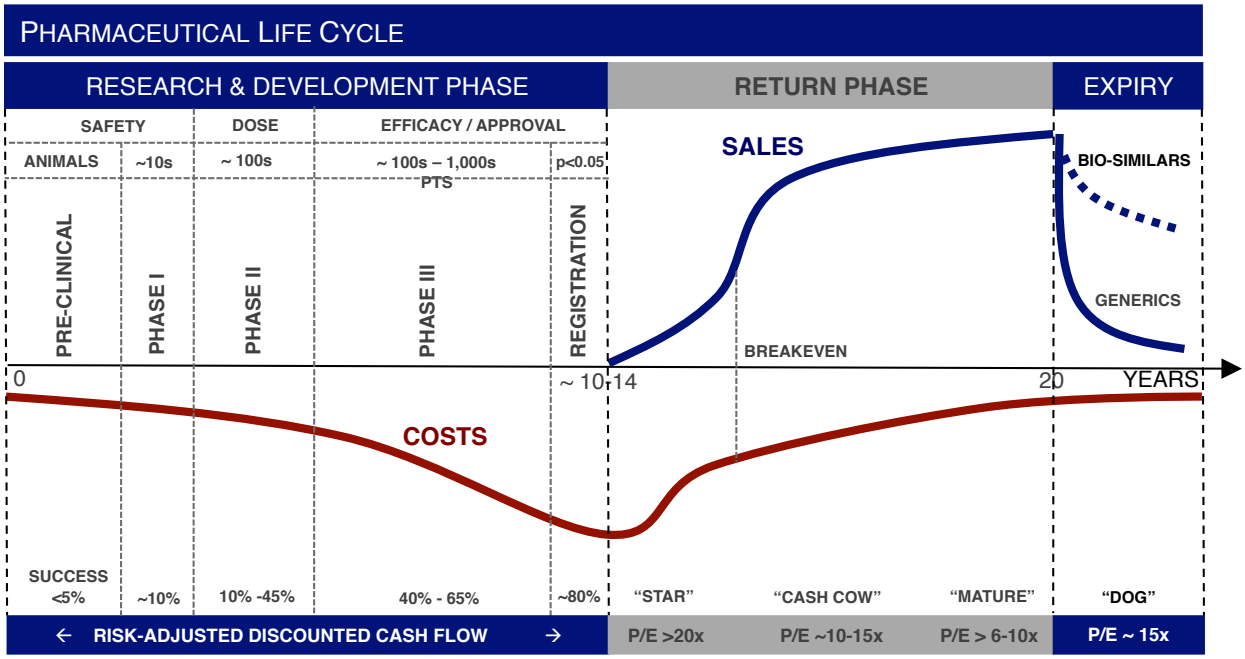
THIOGENESIS THERAPEUTICS										SHARE PRICE (CAD)	0.75	
RATIOS	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
P/E			**-6.8x**	**-6.5x**	**1.3x**	**0.4x**	**0.1x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**
P/S					**0.8x**	**0.2x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**
P/NAV			**-13.8x**	**-4.6x**	**2.0x**	**0.3x**	**0.1x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**
EV/EBITDA			**-5.0x**	**-4.7x**	**1.0x**	**0.3x**	**0.1x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**
PER SHARE DATA (CAD)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
EARNINGS	**-0.12**	**-0.05**	**-0.11**	**-0.12**	**0.57**	**2.01**	**10.30**	**21.27**	**36.56**	**51.24**	**62.37**	**71.19**
CHANGE (%)		-63%	138%	5%	-590%	253%	413%	107%	72%	40%	22%	14%
CASH	**0.17**	**0.10**	**0.14**	**0.01**	**0.60**	**2.72**	**13.54**	**35.87**	**74.25**	**128.04**	**193.51**	**268.23**
CHANGE (%)		-40%	36%	-94%	6679%	351%	398%	165%	107%	72%	51%	39%
DIVIDENDS	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE	**0.16**	**0.05**	**-0.05**	**-0.16**	**0.37**	**2.23**	**11.79**	**31.55**	**65.50**	**113.08**	**171.01**	**237.12**
CHANGE (%)		-70%	-213%	199%	-326%	508%	429%	167%	108%	73%	51%	39%
BALANCE SHEET (CAD MN)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NET LIQUID FUNDS	**6**	**7**	**9**	**1**	**40**	**179**	**890**	**2'358**	**4'880**	**8'414**	**12'717**	**17'627**
TOTAL ASSETS	**6**	**7**	**9**	**1**	**40**	**179**	**890**	**2'358**	**4'880**	**8'414**	**12'717**	**17'627**
SHAREHOLDERS' EQUITY	**6**	**3**	**-4**	**-11**	**24**	**147**	**775**	**2'073**	**4'304**	**7'431**	**11'238**	**15'583**
CHANGE (%)	-663%	-47%	-213%	199%	-326%	508%	429%	167%	108%	73%	51%	39%
RETURN ON EQUITY (%)	-66%	-89%	189%	67%	144%	84%	81%	63%	52%	42%	34%	28%
FINANCIAL DEBT	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
FINANCIAL DEBT AS % OF TOTAL ASSETS	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
EMPLOYEES	**5**	**5**	**8**	**12**	**20**	**21**	**21**	**22**	**22**	**23**	**23**	**24**
CHANGE (%)		0%	60%	50%	67%	5%	2%	2%	2%	2%	2%	2%
CASH FLOW STATEMENT (CAD MN)	**2022**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NET PROFIT / (LOSS) BEFORE TAX	**-4**	**-3**	**-7**	**-8**	**40**	**140**	**712**	**1'468**	**2'523**	**3'535**	**4'303**	**4'911**
DEPRECIATION & AMORTIZATION	0	0	0	0	0	0	0	0	0	0	0	0
OTHER NON-CASH ITEMS	2	-1	0	0	0	0	0	0	0	0	0	0
CASH FLOW	**-2**	**-3**	**-7**	**-8**	**40**	**140**	**712**	**1'468**	**2'523**	**3'535**	**4'303**	**4'911**
NET INCREASE/(DECREASE) IN WORKING CAPITAL	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1
OPERATING FREE CASH FLOW	**-2**	**-4**	**-8**	**-8**	**39**	**139**	**711**	**1'468**	**2'522**	**3'535**	**4'302**	**4'910**
NET CASH FLOWS FROM INVESTING ACTIVITIES	0	0	0	0	0	0	0	0	0	0	0	0
NET CASH USED IN OPERATING ACTIVITIES	**-2**	**-4**	**-8**	**-8**	**39**	**139**	**711**	**1'468**	**2'522**	**3'535**	**4'302**	**4'910**
NET CASH FLOWS FROM FINANCING ACTIVITIES	8	5	10	0	0	0	0	0	0	0	0	0
EFFECT OF EXCHANGE RATE CHANGES ON CASH	0	0	0	0	0	0	0	0	0	0	0	0
NET INCREASE/(DECREASE) CASH & CASH EQUIVALENTS	**6**	**0**	**2**	**-8**	**39**	**139**	**711**	**1'468**	**2'522**	**3'535**	**4'302**	**4'910**

ESTIMATES AS OF 11 JANUARY 2024 SOURCE: VALUATIONLAB ESTIMATES

NOTE: Thiogenesis' estimated cash and cash equivalents of CAD 7.0 mn (31 December 2023) with an additional cash need of approximately CAD 9 mn should be sufficient to reach the next major value inflection points for key compound TTI-0102 in MELAS, Rett syndrome, and pediatric NASH.

Pharmaceutical life cycle

To determine the value of a prescription (bio)pharmaceutical compound, it is critical to understand its life cycle. Fortunately, all compounds follow the same life cycle. The clock starts ticking after the compound is patented, providing 20 years of protection from generic competition. Market exclusivities can extend this protection period. The average Research & Development Phase takes 10-14 years, leading to an effective Return Phase of 6-10 years. The Development Phase has 3 distinct Phases, focused on safety (Phase I), dose (Phase II) and efficacy/clinical benefit (Phase III). The compound is filed for registration/approval at the FDA (US) or EMA (EU). The Return Phase is characterized by a star, cash cow, and mature phase. After patent expiry (or loss of market exclusivity) generic manufacturers may copycat the branded prescription drug, at significantly lower costs, leading to a sales and earnings implosion of the branded drug.



SOURCE: VALUATIONLAB

Success probabilities & Royalties

In our risk-adjusted NPV calculations, we use standardized success probabilities based on historical clinical success rates. The success rate increases as the project progresses through development. Sales and earnings forecasts are based on the clinical and competitive profile of the compound. The more advanced the compound is, the more accurate the forecasts become as the target market can be defined. We conservatively exclude projects that lack Phase IIa proof-of-concept data in our valuations.

SUCCESS PROBABILITIES & ROYALTIES

DEVELOPMENT STAGE	AIM	WHAT / WHO	SUCCESS PROBABILITY (%)	COSTS (USD MN)	ROYALTIES (%)
PRE-CLINICAL	SAFETY & PHARMACOLOGY DATA	LAB TESTS / ANIMALS - NO HUMANS!	< 5	3	
PHASE I	SCREENING FOR SAFETY	HEALTHY VOLUNTEERS (10'S)	5-15	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-20		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	15-35	5	5-15
PHASE IIB	OPTIMAL DOSAGE	PATIENTS WITH DISEASE (100'S)	20-45	5-10	
PHASE III	EVALUATE OVERALL BENEFIT/RISK	PATIENTS WITH DISEASE (1,000'S)	40-65	> 20-1,000	10-25
REGULATORY FILING	DETERMINE PHYSICIAN LABELING	CLINICAL BENEFIT ASSESSMENT	80-90		
APPROVAL	MARKETING AUTHORIZATION	PHYSICIANS FREE TO PRESCRIBE	100		15-30

SOURCE: VALUATIONLAB, TUFTS, FDA, EMA, CLINICALTRIALS.GOV

Important Research Disclosures

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Our financial analyses are based on the "Directives on the Independence of Financial Research" issued by the Swiss Bankers Association in January 2008.

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Risk Qualification

Speculative	less than 1 year cash and breakeven beyond 1 year
High Risk	profitable within 2 years and 1 approved product/key indication (patent expiry > 5 years)
Medium Risk	profitable and/or sales from at least 2 marketed products/key indications (patent expiry > 5 years)
Low Risk	profitable and sales from >2 marketed products/key indications (patent expiry > 5 years)

Analyst Certification

The research analyst(s) identified on the first page of this research report hereby attest that all of the views expressed in this report accurately reflect their personal views about any and all of the subject securities or issuers. In order to ensure the independence of our research analysts, and their immediate household, are expressly prohibited from owning any securities in the valuationLAB AG research universe, which belong to their sector(s). Neither the research analyst nor his/her immediate household serves as an Officer, Director or Advisory Board Member of **Thiogenesis Therapeutics Corp.**