EGETIS THERAPEUTICS

WE CARE

FOR THE RARE

Corporate presentation

November 2025

Emcitate® (tiratricol) launched in Germany in May 2025

Rolling NDA to commence Dec 2025 based on currently available clinical data

For investors and analysts only

Disclaimer

Tiratricol is an investigational drug and has not been approved by the U.S. Food and Drug Administration (FDA). Its safety and efficacy have not been established in the U.S.

THIS PRESENTATION AND ITS CONTENTS ARE NOT FOR RELEASE, PUBLICATION OR DISTRIBUTION, IN WHOLE OR IN PART, DIRECTLY OR INDIRECTLY, IN OR INTO OR FROM THE UNITED STATES OF AMERICA, CANADA, AUSTRALIA, JAPAN OR ANY JURISDICTION WHERE SUCH DISTRIBUTION IS UNLAWFUL.

IMPORTANT: You must read the following before continuing. The following applies to this document, the oral presentation of the information in this document by Egetis Therapeutics AB (the "Company") or any person on behalf of the Company, and any question-and-answer session that follows the oral presentation (collectively, the "Information"). In accessing the Information, you agree to be bound by the following terms and conditions.

The Information is not intended for release, publication or distribution, in whole or in part, directly or indirectly, in or into or from the United States of America, Canada, Australia, Japan or any other jurisdiction where such distribution would be unlawful. This presentation is not a prospectus or similar document and it has not been approved, registered or reviewed by the Swedish Financial Supervisory Authority nor any governmental authority or stock exchange in any jurisdiction.

The Information has been prepared by the Company and is intended to present background information on the Company, its business and the industry in which it operates. The Information contains summary information only and does not purport to be comprehensive and is not intended to be (and should not be used as) the sole basis of any analysis or other evaluation. The Information does not constitute or form part of and should not be construed as an offer or the solicitation of an offer to subscribe for or purchase securities of the Company, and nothing contained therein shall form the basis of or be relied on in connection with any investment activity. The Company shall not have any liability whatsoever (in negligence or otherwise) for any loss whatsoever arising from any use of the Information or otherwise arising in connection with this presentation.

By accessing this Information, you represent that such access does not violate any registration requirements or other legal restrictions in the jurisdiction in which you reside or conduct business. It is especially noted that the Information may not be accessed by persons within the United States or "U.S. Persons" (as defined in Regulation S under the Securities Act of 1933, as amended (the "Securities Act") unless they are qualified institutional buyers "QIBs" as defined in Rule 144A under the Securities Act. By accessing the Information, you represent that you are (i): a non-U.S. person that is outside the United States or (ii) a QIB. Further, the Information may not be accessed by persons within the United Kingdom unless they are persons with professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 as amended (the "Order"), a "qualified investors" falling within Article 2(e) of Regulation (EU) 2017/1129 as it forms part of English law by virtue of the European Union (Withdrawal) Act 2018 ("EUWA"), or high net worth entities falling within Article 49(2)(a) to (d) of the Order (each a "Relevant Person"). By accessing the Information, you represent that you are: (i) outside the United Kingdom or (ii) a Relevant Person.

The Information contains forward-looking statements. All statements other than statements of historical fact included in the Information are forward-looking statements. Forward-looking statements give the Company's current expectations and projections relating to its financial condition, results of operations, plans, objectives, future performance and business. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could" and other words and terms of similar meaning or the negative thereof. Such forward-looking statements involve known and unknown risks, uncertainties and other important factors beyond the Company's control that could cause the Company's actual results, performance or achievements to be materially different from the expected results, performance or achievements expressed or implied by such forward-looking statements. Such forward-looking statements are based on numerous assumptions regarding the Company's present and future business strategies and the environment in which it will operate in the future. As a result, you are cautioned not to place undue reliance on such forward-looking statements.

No representation, warranty or undertaking, express or implied, is made by or on behalf of the Company as to, and no reliance should be placed on, the fairness, accuracy, completeness or correctness of the Information or the opinions contained therein. The Information has not been independently verified and will not be updated. The Information, including but not limited to forward-looking statements, applies only as of the date of this document and is not intended to give any assurances as to future results. The Company expressly disclaim any obligation or undertaking to disseminate any updates or revisions to the Information, including any financial data or forward-looking statements, and will not publicly release any revisions it may make to the Information that may result from any change in the Company's expectations, any change in events, conditions or circumstances on which these forward-looking statements are based, or other events or circumstances arising after the date of this document. Market data used in the Information not attributed to a specific source are estimates of the Company and have not been independently verified.

WE CARE

FOR THE RARE

1.

An integrated orphan drug company, focusing on late-stage development and commercialization

Egetis: building an orphan drug commercial stage company

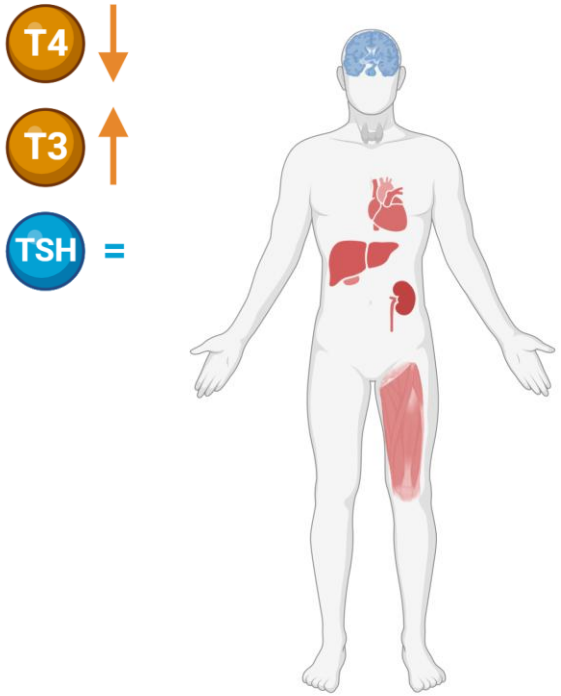
1. Focus on orphan diseases with proprietary asset **Emcitate®** *(tiratricol)* for the treatment of MCT8 deficiency
   Emcitate has been supplied to over 230 patients in over 25 countries including US, EU
2. Approved in EU in Feb 2025. Launched in Germany May 1, 2025
   Rolling NDA to commence Dec 2025 based on currently available clinical data
3. The first and only approved drug for the treatment of MCT8 deficiency
   A significant market opportunity & potential for expansion into RTH-beta
4. Launch through focused in-house commercial organization in the EU and US with partnership for RoW (Japan: Fujimoto, Türkiye: Er-Kim)
5. A strong team with late-stage orphan clinical development, registration and commercialization experience

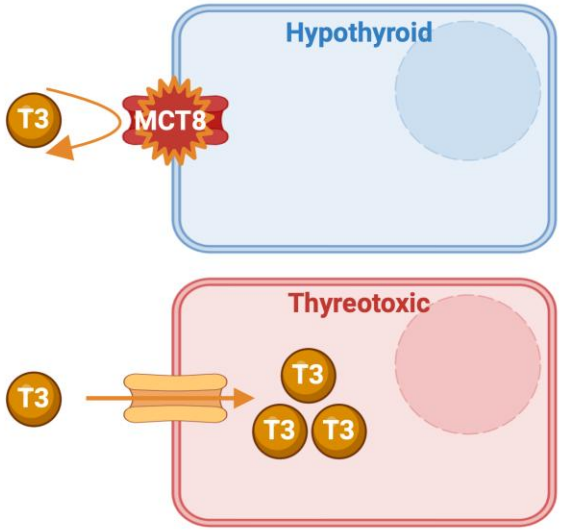
Strong regulatory status

BTD	**Breakthrough Therapy Designation - FDA**
ODD	**Orphan Drug Designation – EMA & FDA** Market exclusivity 10y (EU) & 7y (US)
Fast track	**Fast track designation - FDA**
PRV	**Rare pediatric disease designation - FDA** **Priority Review Voucher upon approval**

Listed on NASDAQ Stockholm (EGTX)
HQ in Stockholm, Sweden
~40 FTEs

MCT8 deficiency results in dysfunctional thyroid hormone trafficking





MCT8 deficiency results in simultaneous too high and too low thyroid hormone levels – causing system wide issues

MCT8 deficiency key features

Estimated incidence: 1 per 70k male births

Median onset of symptoms: 4 months

Median age of diagnosis: 10 months

Median life expectancy: 35 years

Patients dying in childhood: ~30%

Main cause of mortality: Sudden cardiac death

Severe underweight: 75%

Cardiac arrhythmias (PAC): 76%

Hypotonia, hypertonia
& persistence of primitive reflexes: 90%

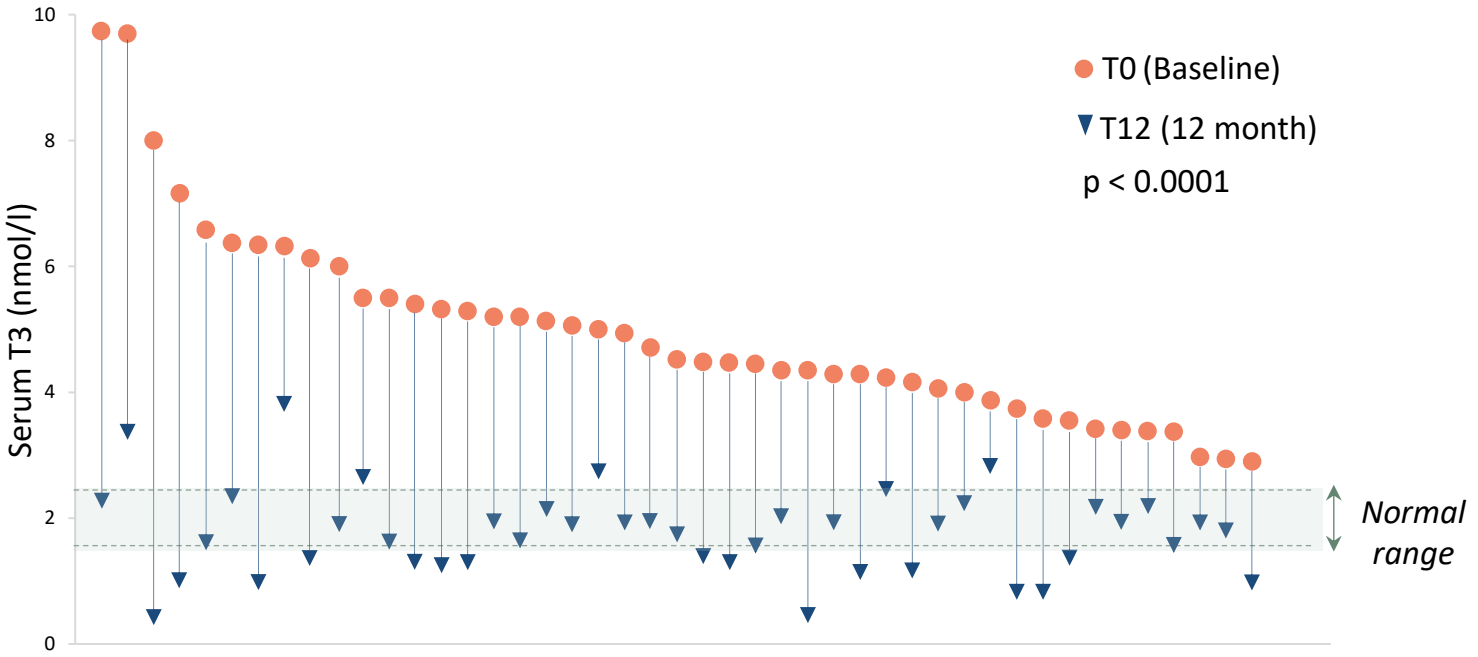
Severe intellectual disability: 100%

Ability to sit independently: 8%

Life long 24-hour care: 100%

Tiratricol treatment in patients with MCT8 deficiency has been shown to be associated with survival benefits

In the Triac Trial I, tiratricol reached target level serum T3 & improvements in clinically relevant outcome measures



Tiratricol has been shown to be associated with a 3x lower risk of mortality in patients with MCT8 deficiency

Retrospective real-world cohort study in >300 patients - Abstracts Aug. 2024 & May 2025

Key demonstrated clinical results

- ✓ Significant and durable reduction of T3 levels within the normal range
- ✓ Normalization of thyrotoxicosis in patients of all ages
- ✓ Improvement of bodyweight and cardiovascular status
- ✓ Beneficial effects are maintained or continue to improve over time, up to six years
- ✓ Benign safety profile

Source: Groeneweg et al; Lancet D&E 2019

Emcitate/tiratricol regulatory pathway in EU/US

Robust data set in an ultra rare genetic disease

Triac Trial I	EMC cohort study	Natural history	Triac Trial II	EMC survival study	ReTRIACt
N=46	N=67	N=151	N=22	N>600	N=15
• Completed 2018 (Groeneweg, 2019) • Open-label, international, multi-centre study	• Completed 2021 (van Geest, 2022) • N= 27 from Triac Trial I & N= 40 new pts from managed access program	• Retrospective data, 2003 to 2019 (Groeneweg, 2020)	• Open-label, international, multi-centre study • Focus on neurocognition; did not meet its primary endpoints • 96 weeks safety data in young patients	• Basis for Breakthrough Therapy Designation by FDA • Comparing treated vs untreated patients on survival • Treatment with tiratricol (Emcitate®) is **associated with a 3x lower risk of mortality**	• Placebo-controlled withdrawal study • SAP revised • Topline results expected Q4 2025 • Complementary data for the NDA

Data included in EMA MAA – EC approval Feb 2025

Data to be included in FDA NDA

EMC: Erasmus Medical Center; SAP: Statistical Analysis Plan

Breakthrough Therapy Designation (BTD) granted by the FDA

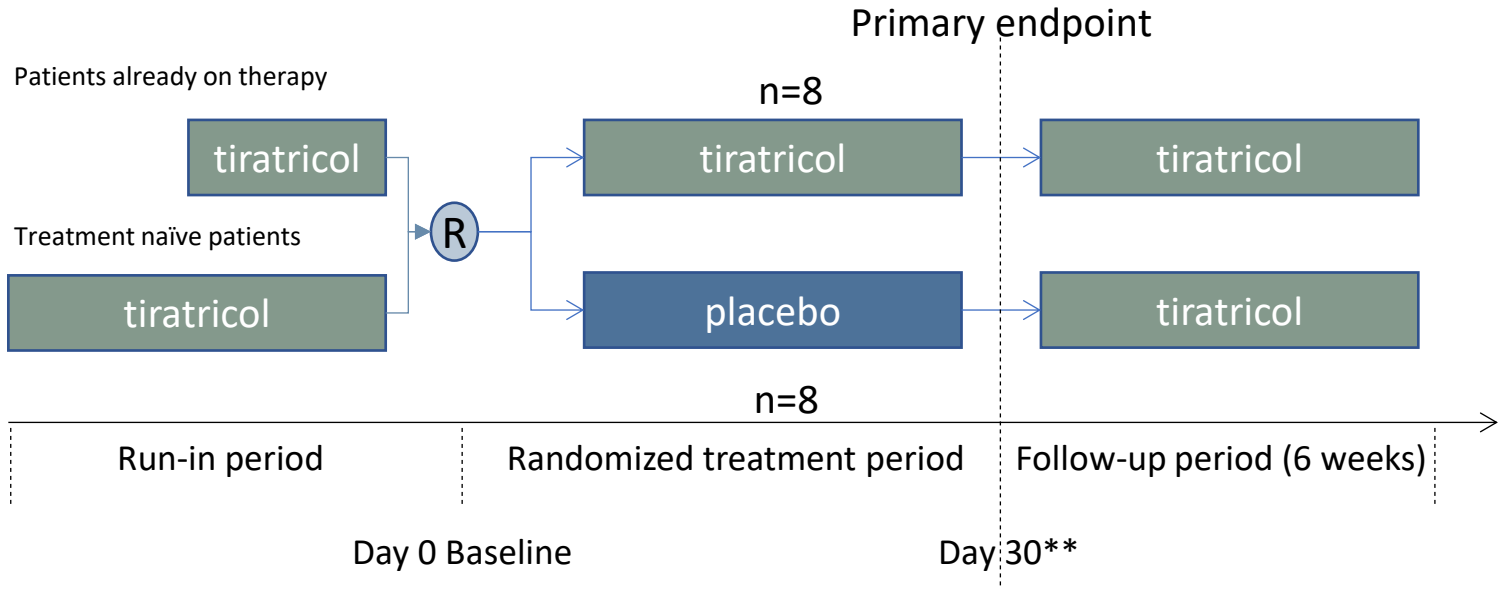
- The BTD was granted (July 2025) based on the Agency's review of Egetis' detailed analysis of the entire survival data set from the international real-world cohort study by the Erasmus University Medical Center, demonstrating a significant and substantial improvement in survival in tiratricol treated vs untreated MCT8-deficiency patients

- FDA Breakthrough Therapy Designation underscores both the urgent need for an effective treatment for patients with MCT8 deficiency and the clinically meaningful evidence demonstrated to date with tiratricol

Design of the ReTRIACt trial (status October 23, 2025)

Requested by and agreed with the FDA

- A 30-day, randomized placebo-controlled withdrawal study in 15 patients
- The study allowed for inclusion of patients that were already on therapy and patients that were treatment naïve
- Treatment naïve patients require a longer run-in period to stabilize T3 levels around normal range before randomization



- There are 15 evaluable patients in the ReTRIACt trial
- As recommended by the FDA, the Statistical Analysis Plan for the ReTRIACt trial will be revised and the study will be closed
- Complementary study to the survival data and other clinical components in the NDA
- Topline results expected in the fourth quarter of 2025. Data accrued to date will be included in the NDA

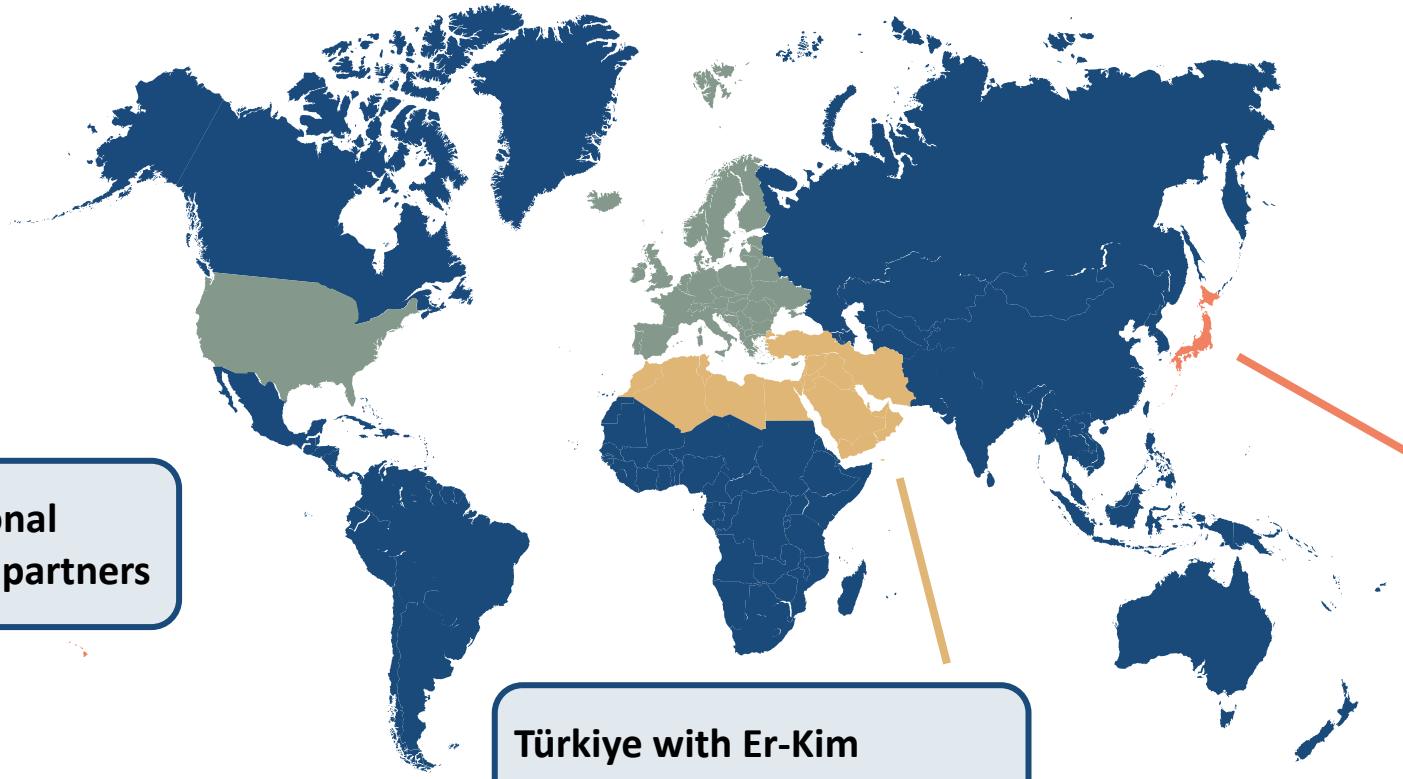
Initiation of rolling NDA submission planned in December 2025, with NDA completion early 2026

BTD: Breakthrough Therapy Designation

Emcitate launch by Egetis and partners

Executing the US & European market preparations and launches through the Egetis team

To optimize the launch, we will focus our own resources on US and Europe (> 70% of sales for most ultra-orphans)



Optimizing additional countries through partners

Türkiye with Er-Kim MENA partnering dialogues

Japan license deal with Fujimoto

A phased EU launch through in-house commercial organization started in Germany May 1

Pricing & Reimbursement (P&R) strategy execution in 2 waves, starting with EU4

Wave 1

France, Germany, Italy, Spain

Wave 2

Phased on a country-by-country approach

Rest of Europe

Pricing & Reimbursement processes

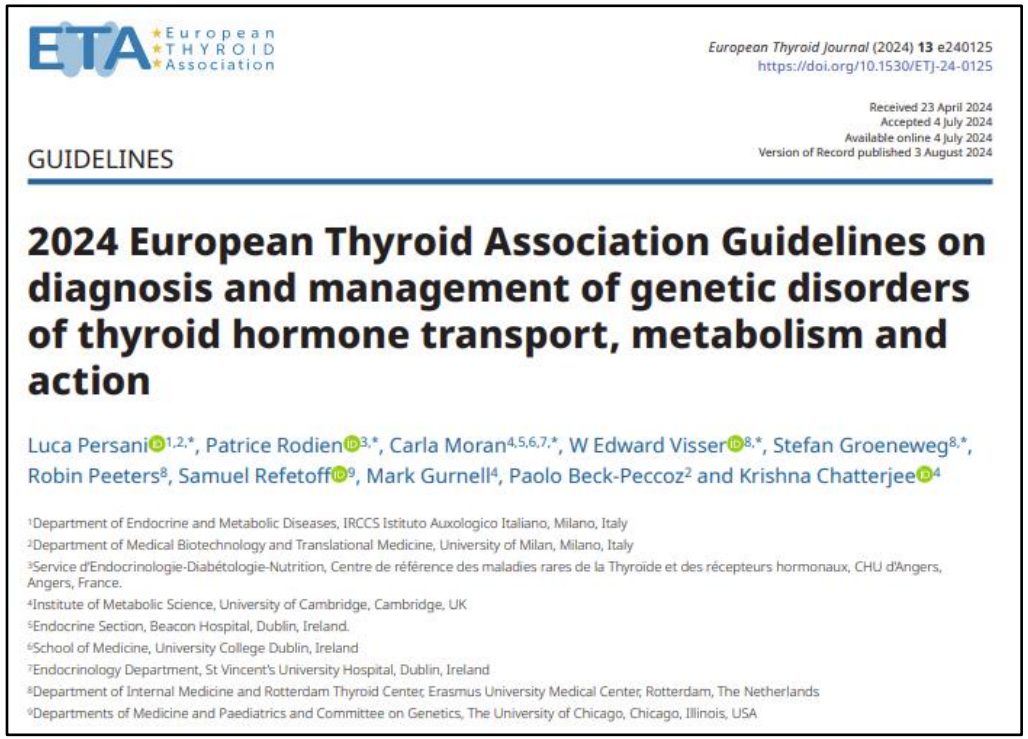
Deliver the *Emcitate* clinical and economic value proposition in P&R processes, outlining:

- MCT8 deficiency and its rarity
  - Summarizing available literature
- High burden of MCT8 deficiency
  - Confirmed by Egetis sponsored Caregiver study
- Significant unmet medical need
  - Emcitate the first & only approved treatment
- Benefit of treatment
  - Supported by publications & ETA guidelines*

*European Thyroid Association guidelines published 2024

European Thyroid Association (ETA) recommends tiratricol as long-term therapy for all patients with MCT8 deficiency

- ETA recommends the **use of tiratricol as long-term therapy for all patients** with MCT8 deficiency, and for certain patients with RTH-beta.
- Inaugural 2024 Guidelines were commissioned by the Executive Committee of the ETA and developed by an independent team of experts.



ETA European THYROID Association

European Thyroid Journal (2024) **13** e240125
https://doi.org/10.1530/ETJ-24-0125

Received 23 April 2024
Accepted 4 July 2024
Available online 4 July 2024
Version of Record published 3 August 2024

GUIDELINES

2024 European Thyroid Association Guidelines on diagnosis and management of genetic disorders of thyroid hormone transport, metabolism and action

Luca Persani[1,2,*], Patrice Rodien[3,*], Carla Moran[4,5,6,7,*], W Edward Visser[8,*], Stefan Groeneweg[8,*], Robin Peeters[8], Samuel Refetoff[9], Mark Gurnell[4], Paolo Beck-Peccoz[2] and Krishna Chatterjee[4]

[1]Department of Endocrine and Metabolic Diseases, IRCCS Istituto Auxologico Italiano, Milano, Italy
[2]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milano, Italy
[3]Service d'Endocrinologie-Diabétologie-Nutrition, Centre de référence des maladies rares de la Thyroïde et des récepteurs hormonaux, CHU d'Angers, Angers, France.
[4]Institute of Metabolic Science, University of Cambridge, Cambridge, UK
[5]Endocrine Section, Beacon Hospital, Dublin, Ireland.
[6]School of Medicine, University College Dublin, Ireland
[7]Endocrinology Department, St Vincent's University Hospital, Dublin, Ireland
[8]Department of Internal Medicine and Rotterdam Thyroid Center, Erasmus University Medical Center, Rotterdam, The Netherlands
[9]Departments of Medicine and Paediatrics and Committee on Genetics, The University of Chicago, Chicago, Illinois, USA

Germany launch execution delivering early wins in parallel with pricing and reimbursement (P&R) process

- Emcitate launched and available in Germany as of May 1
- P&R process initiated on April 30, to be finalized by May 2026
- Sales of commercial Emcitate packs initiated in parallel with the ongoing P&R process
  - Almost all managed access patients converted to commercial packs
  - New patients initiated
- Productive engagements with physicians at center meetings and at congresses
  - Exhibited at 7 regional medical congresses in 2025
- For broader physician reach, complementing in-person meetings with promotional and educational initiatives through other channels, such as
  - Virtual meetings, web, mailings, and publications

US: Steady, well-executed market preparations supporting launch readiness

Patient Journey Insights

- Using real-world data analytics to gain a more granular view of the diagnostic journey and patterns of disease management
- Identify actionable signals that can support earlier recognition and referral of patients
- In total > 100 diagnosed patients identified in the US

Expanded Access Program

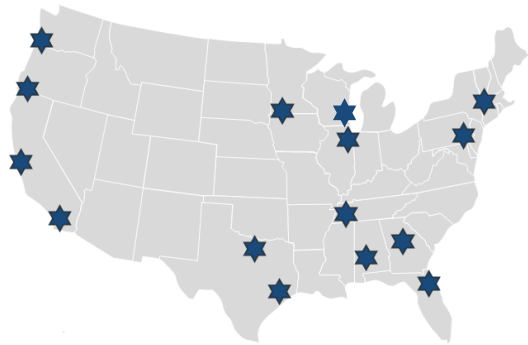
- Active at 15 sites nationwide
- Provides therapy today and builds real-world readiness

Market Access Preparations

- Core focus on speed & breadth of coverage at launch
- Robust evidence package, clear payer pathways

Launch Infrastructure

- Expanding field medical presence
- Strengthening rare disease ecosystem engagement



EAP sites

US: Balancing Annual Treatment Costs and Broad Access

Analogues

Product	Disease	Estimated annual treatment cost (WAC)
Skyclarys® *Small molecule*	Friedreich's ataxia	~$400K
Procysbi® *Small molecule*	Nephropathic cystinosis	~$550K
Ravicti® *Small molecule*	Urea cycle disorder	~$750K
Exondys® *Antisense oligonucleotide*	Duchenne muscular dystrophy	~$750K

Access

Less restrictive
- Prior Authorization to label
- Genetic Test Attestation/documentation
- Specialist prescribing

More restrictive
- Prior Authorization beyond label
- Attestation of clinical benefit
- Medical exception with appeal

Strong financial foundation for strategic execution

Solid cash position

- **Cash position August 21, 2025**: SEK 203 million
- **Number of outstanding shares:** 395,161,938
- **Market Cap:** ~SEK 2.6 billion* (~USD 274 million)
- **Listing venue:** Nasdaq Stockholm, Main Market; **Ticker:** EGTX

Largest shareholders

			↓ Capital
1	+	Frazier Life Sciences	16.73%
2	+	Peter Lindell	10.09%
3	+	Peder Walberg	7.33%
4	+	Fjärde AP-fonden	7.22%
5		Avla Holding AB	4.50%
6	+	The Invus Group	4.19%
7		Unionen	3.52%
8		Avanza Pension	2.84%
9		RegulaPharm AB	2.68%
10	+	Linc AB	2.10%
11	+	Woodline Partners LP	1.49%
12	+	Swedbank Robur Fonder	1.38%

Directed share issue Oct. 2025 of SEK 183m (USD 19m)

- Oversubscribed with participation from new & existing investors
- US biotech investors: Frazier Life Sciences, Invus, Petrichor & Woodline
- Swedish investors: Fjärde AP-fonden, Cidro Förvaltning (Peter Lindell), Linc & others

Note: * October 31, 2025

Value enhancing key milestones 2025-2026

Emcitate® — **2025-2026**

MCT8 deficiency

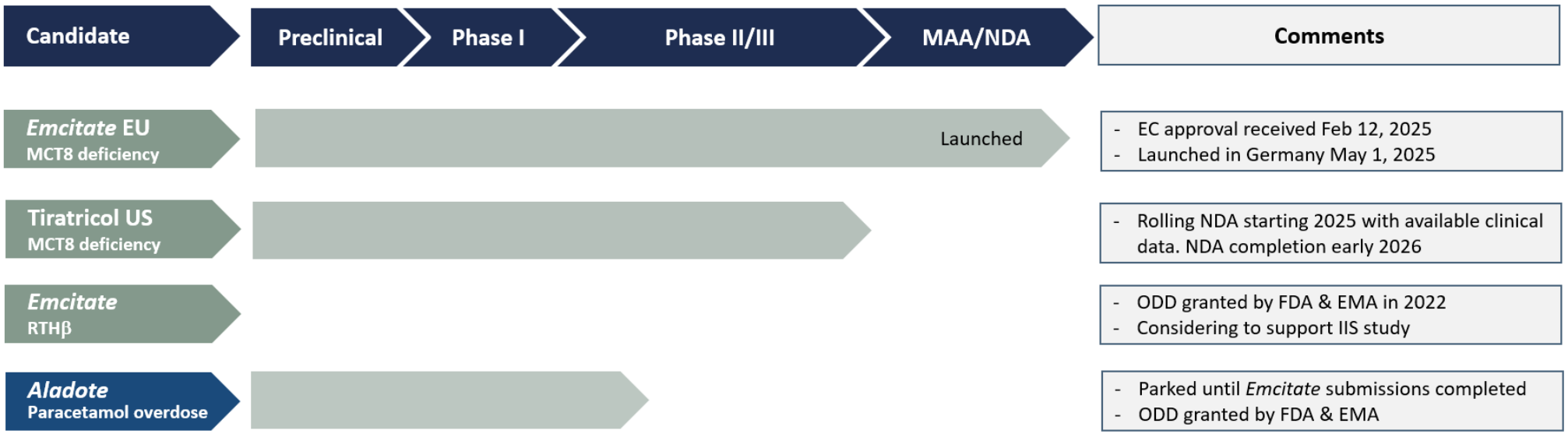
- ✓ EU launch, in Germany, May 1, 2025
- ✓ Break Through Designation granted by FDA
- ✓ Türkiye partnership signed with Er-Kim
- Topline results ReTRIACt Q4 2025
- Rolling submission of US NDA to start Dec 2025
- NDA completion early 2026
- Middle East, North Africa partnership/s
- Japan – Development plan agreed with PMDA
- US Patent granted - Processes and compounds
- US approval and launch
- US Rare Pediatric Disease Priority Review Voucher

RTH-beta

- Potential initiation of Investigator Initiated Study - Egetis Industry collaborator

Pipeline Overview

Emcitate® (tiratricol) – Launched in Germany May 1, 2025



EC: European Commission; IIS: Investigator Initiated Study; MAA: Marketing Authorisation Application (EU); NDA: New Drug Application (USA); ODD: Orphan Drug Designation; RTHβ: Resistance to Thyroid Hormone beta

Building a sustainable orphan drug company

- Successfully develop *Emcitate* for EU & US approvals in 2025/26 and potentially *Aladote* post 2026
- Commercialize *Emcitate* and *Aladote* through an inhouse organization in Europe/ North America and partnerships in RoW
- Realize the full potential of our products via life-cycle management
- Ensure fast and broad access to our products for the benefit of patients worldwide
- Identify further assets that address the significant unmet medical need for patients with rare diseases
- Provide an open culture that encourages Collaboration, Courage & Commitment
- Egetis financial objective is to create increased value for shareholders in the long term

To bring unique therapies to patients with rare diseases that improve and extend life

To create value for patients, society and shareholders by developing and providing a portfolio of unique products for the treatment of rare diseases with substantial medical need

Appendix 1

Overview of MCT8 deficiency

MCT8 deficiency results in dysfunctional thyroid hormone trafficking

MCT8 deficiency has two co-manifestations

New Research Sheds Light on Thyroid Hormone Transport

- In 2003, MCT8 was identified as one of the first thyroid hormone transporters
  - Previously, thyroid hormone was incorrectly believed to be able to passively cross cellular membranes, without the need for a specific transporter
- Several additional transporters have been identified with preferential distribution across different tissue types and cells

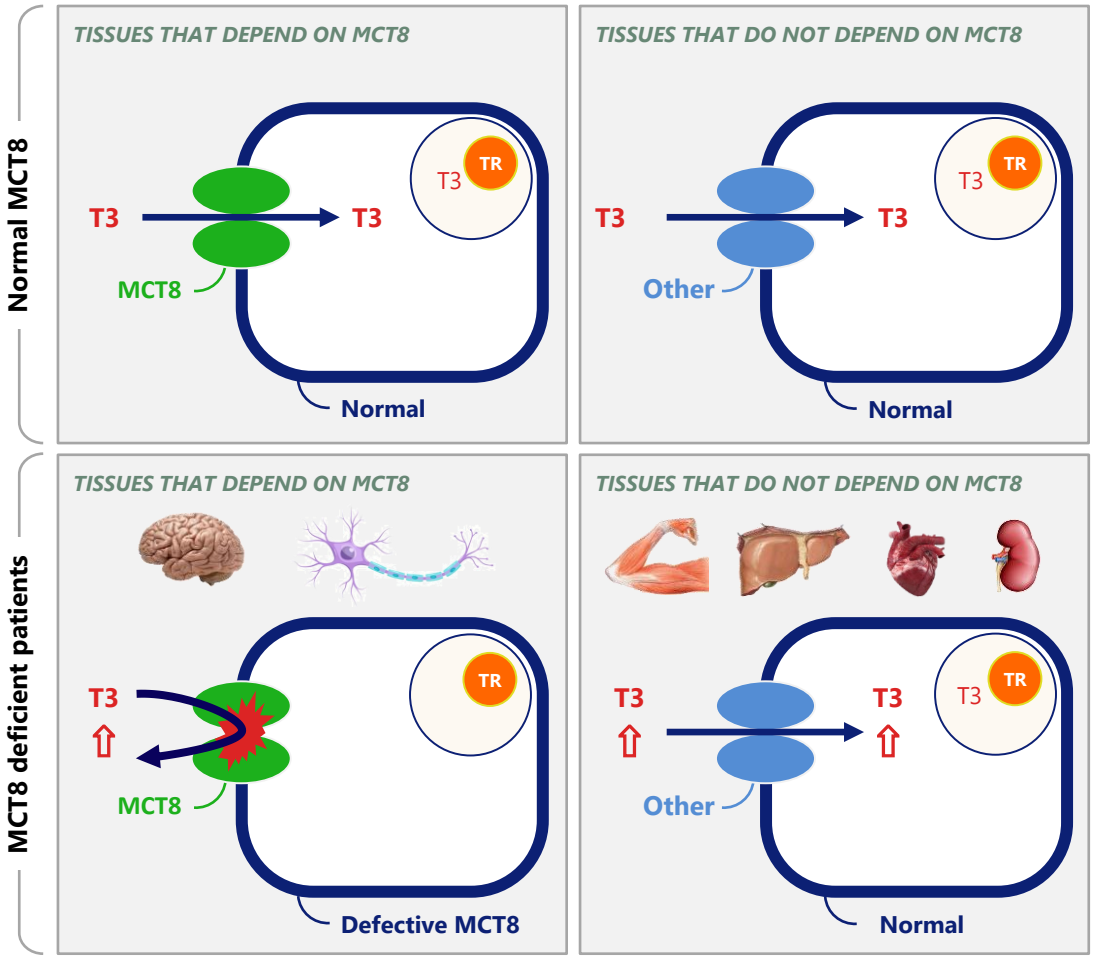
MCT8 Plays a Key Role in Neurocognitive Development

- MCT8 is the only thyroid hormone transporter in the cells of the blood brain barrier and neurons
  - The human brain is dependent on thyroid hormone for its normal development. Absence of thyroid hormone in the CNS leads to disruption of neurocognitive development and results in severe neurocognitive and motor impairment

And Causes Many Additional Symptoms

- Disrupted thyroid hormone homeostasis leads to an increase of peripheral serum T3 levels
- Tissues dependent on transport other than MCT8 suffer from too high levels of thyroid hormone:
  - Increased heart frequency, blood pressure and arrhythmias
  - Severe wasting and weight loss
  - Impaired liver / kidney function
  - Altered bone metabolism and blood lipids
  - Increased risk of sudden and premature death

MCT8 deficiency results in simultaneous too high and too low thyroid hormone levels – causing system wide issues



MCT8 deficiency: a detrimental condition with significant unmet medical need

What is MCT8 deficiency?

- Genetic X-linked disorder
- Impaired thyroid hormone trafficking across cellular membranes
- MCT8 is a key thyroid hormone transporter in the body
- Incidence 1:70,000 males

Patients with MCT8 Deficiency[1)]

What does it mean?

- Non-functional MCT8 protein: T3 cannot cross blood-brain-barrier
- Low amounts of thyroid hormone in the brain & CNS
- Disrupted feedback loop results in a compensatory increase in circulating thyroid hormone

- Simultaneous too high & too low thyroid hormone in different tissues

What are the challenges?

- Patients appear normal at birth
- Initial symptoms within the first months of life
- Severe intellectual disability
- Most patients never able to sit or walk; limited ability to communicate
- Life-long morbidity: agitation, CV symptoms, wasting & impaired life expectancy

- Heavily dependent on caregivers resulting in very high disease burden

How do you manage the disease?

- No available therapy
- Easy diagnosis once considered with readily available, low-cost lab-test
- Large proportion of patients remain undiagnosed with significant delay to diagnosis

- Significant unmet medical need: humanitarian, health economic, societal

Quick facts from natural history[2]

Median onset of symptoms: **4 months**

Median age of diagnosis: **10 months**

(prior to 2017: 24 months)

Patients surviving into adulthood: **70%**

Severe intellectual disability: **100%**

Ability to sit independently: **8%**

Hypotonia, hypertonia & persistence of primitive reflexes: **90%**

Severe underweight: **75%**

Cardiac arrythmias (PAC): **76%**

Median life expectancy: **35 years**

Patients dying in childhood: **~30%**

Main cause of mortality: Sudden cardiac death

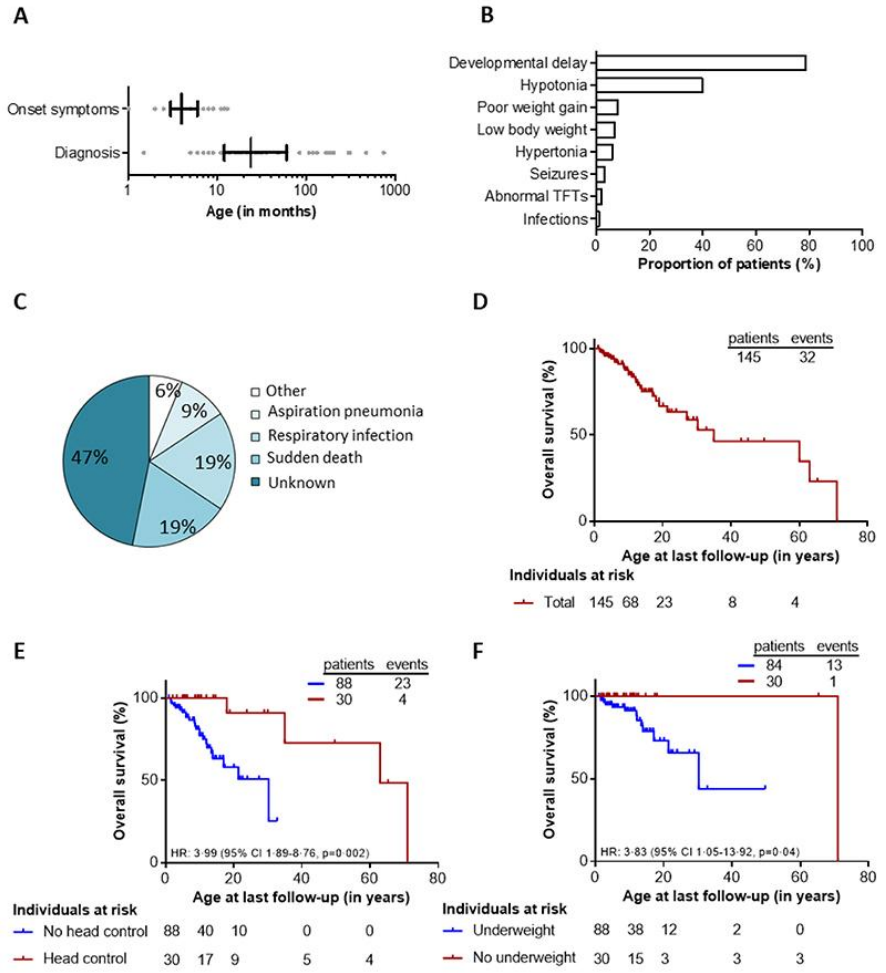
Life long 24-hour care: **100%**

Note: 1) Picture from Schwarz et al; Clin Endocrinol & Met 2007; 2) Groeneweg et al, Lancet Diabetes & Endocrinology, 2020

Natural history study revealed poor survival with a high prevalence of treatable underlying risk factors

An international, retrospective, multicentre cohort study from 2014-2020 in 151 patients

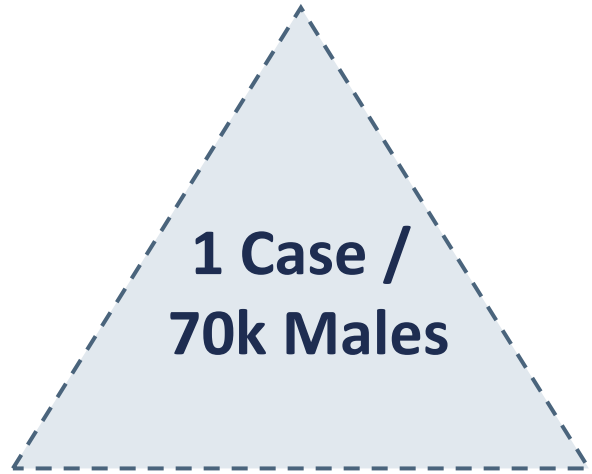
- 151 patients were enrolled with 73 different MCT8 (SLC16A2) mutations
- Median age at diagnosis was 24.0 months
- 21% patients died; the main causes of mortality were pulmonary infection (six patients or 19%) and sudden death (six patients or 19%)
- Median OS was 35.0 years (95% CI 8.3-61.7)
- Individuals who did not attain head control by age 1.5 years had an increased risk of death compared with patients who did attain head control (p=0.0041)
- Patients who were underweight during age 1-3 years had an increased risk for death (p=0.021)
- The few motor & cognitive abilities of patients did not improve with age, as evidenced by the absence of significant correlations between biological age and scores on the Gross Motor Function Measure-88 and Bayley Scales of Infant Development III
- Tri-iodothyronine concentrations were above the age-specific upper limit in 96 (95%) of 101 patients and free thyroxine concentrations were below the age-specific lower limit in 94 (89%) of 106 patients. 59 (71%) of 83 patients were underweight. 25 (53%) of 47 patients had elevated systolic blood pressure above the 90th percentile, 34 (76%) of 45 patients had premature atrial contractions, and 20 (31%) of 64 had resting tachycardia
- The most consistent MRI finding was a global delay in myelination, which occurred in 13 (100%) of 13 patients



Multiple sources lead to consistent MCT8 deficiency incidence estimates

Relevant Sources & Data	Available Data Leads to Consistent MCT8 Deficiency Incidence Estimates
Visser et al., Clinical Endocrinology 2013	• Multiple cohorts of patients with X-linked mental retardation under study • MCT8 deficiency prevalence in studied populations implies a 1:50k-100k Male incidence perimeter
Neonatal Screening - Netherlands	• 140k births & 70k Males a year with 1-2 diagnosed cases a year on average over the past years • Implies more than 1:70k incidence
Triac Trial II - Germany	• 20 months of screening and 400k live births yielded 12 patients below 30 months of age • Implies at least ~1:30k incidence

Supporting our Conservative Estimate



Appendix 2

Emcitate (tiratricol): Mode of action and clinical experience

Emcitate mechanism of action

with clear scientific and mechanistic rationale and established safety profile

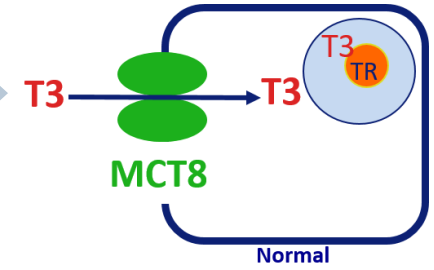
Difference normal MCT8 and deficiency of MCT8

- Thyroid hormone T3 requires transporters such as MCT8 to enter the target cells

Normal MCT8 ✔

- Functional thyroid gland producing T3
- Production of functional MCT8

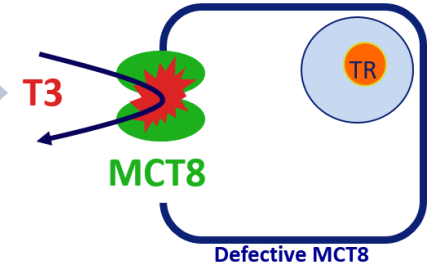
→ T3 cross cell membrane and enters target cell



Mutated MCT8 ✘

- Functional thyroid gland producing T3
- Absence or loss of function of MCT8 on the cell surface

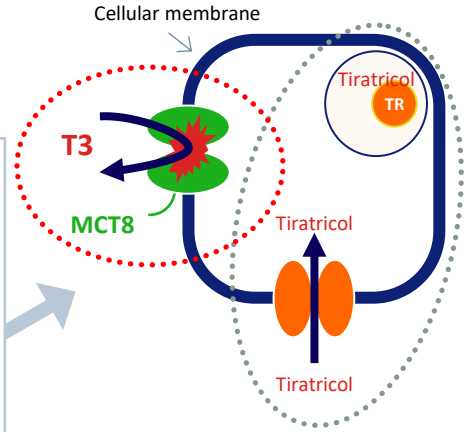
→ T3 cannot cross cell membrane and fails to enter cells



Emcitate (tiratricol) – Addressing MCT8 deficiency

- Tiratricol is a small molecule thyroid hormone T3 analogue
- Unlike T3, tiratricol can cross cellular membranes without a functional MCT8 transporter
- Tiratricol can bypass the problem in patients with MCT8 deficiency, enter MCT8 deficient cells and restore thyroid hormone signalling

***Emcitate* in action**

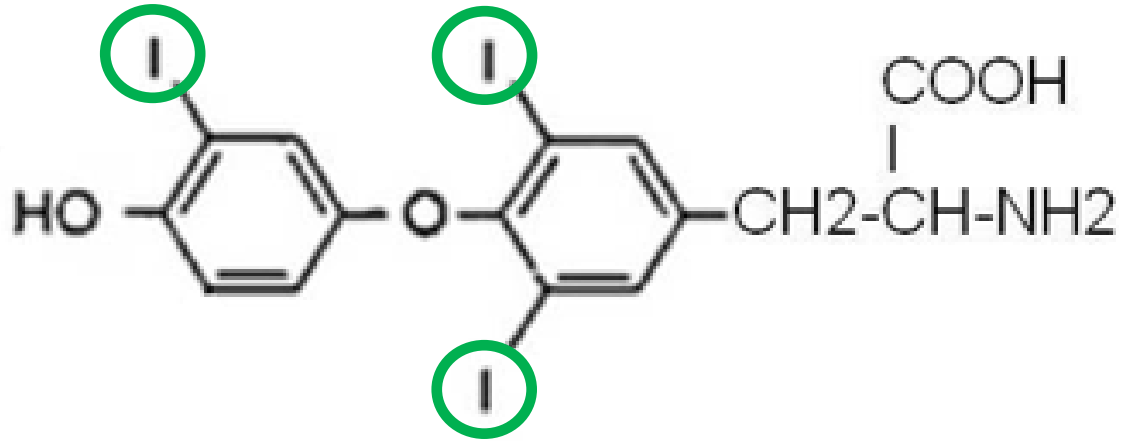


Without a functioning MCT8, T3 is unable to be transported across the cell membrane to enter the target cell ✘

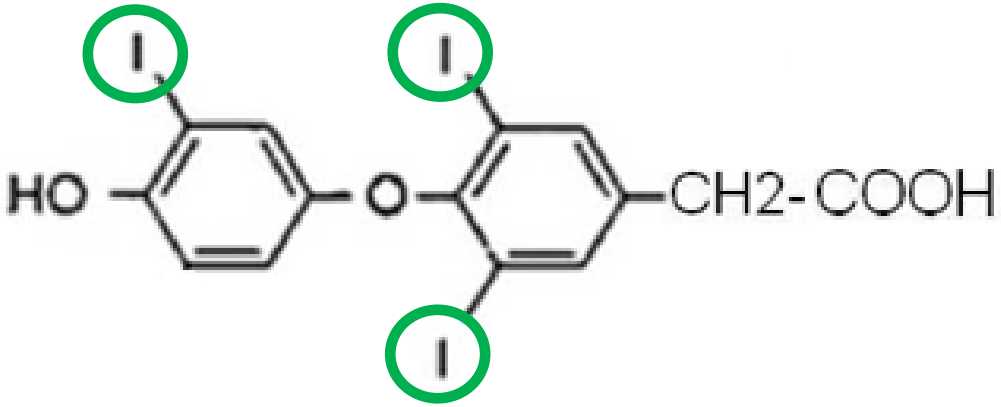
Emcitate can enter the cell without MCT8 and restore thyroid hormone signaling ✔

Discovery of *Emcitate* (Triac, tiratricol)

T3



Triac
(tiratricol)



ROSALIND PITT-RIVERS
M.Sc., Ph.D. Lond.

Preliminary Communication

PHYSIOLOGICAL ACTIVITY OF THE ACETIC-ACID ANALOGUES OF SOME IODINATED THYRONINES

234 THE LANCET] [AUGUST 1, 1953

Overview of completed Phase IIb – Triac Trial I

Primary objective and results

- Evaluate the efficacy and safety of oral administration of tiratricol in male patients with MCT8 deficiency of all ages
- Highly significant primary outcome - Change in T3 serum concentrations
- Safe and tolerable
- Results published in *The Lancet* 2019

Secondary objective and results

- Change in other thyroid hormone function tests, thyrotoxic symptoms and markers
- Significant and clinically relevant effects observed across secondary endpoints

Description

- An international, single-arm, open-label, Phase II trial
- ClinicalTrials.gov identifier: NCT02060474

# of patients

- 46 MCT8 patients in 9 countries

Timetable

- Initiated in 2014 (first patient in)
- Completed in 2018

THE LANCET Articles

Effectiveness and safety of the tri-iodothyronine analogue Triac in children and adults with MCT8 deficiency: an international, single-arm, open-label, phase 2 trial

Stefan Groeneweg, Robin P Peeters, Carla Moran, Athanasia Stoupa, Françoise Auriol, Davide Tonduti, Alice Dica, Laura Paone, Klara Razenkova, Jana Malikova, Adrivan der Walt, Irenaeus F.M. de Coo, Anne McGowan, Greta Lyons, Femke K Aansen, Diana Barca, Ingrid M. van Beynum, Marieke M. van der Knoop, Jurgen Jansen, Martien Manshande*, Roelineke J Lunsing, Stan Nowak, Carsiaan A den Uil, M Carola Zillikens, Frank E Visser, Paul Vrijmoeth, Marie Claire Y de Wit, Nicole I Wolf, Angelique Zandstra, Gautam Ambegaonkar, Yogen Singh, Yolanda B de Rijke, Marco Medici, Enrico S Bertini, Sylvia Depoorter, Jan Lebl, Marco Cappa, Linda De Meirleir*, Heiko Krude, Dana Craiu, Federica Zibordi, Isabelle Oliver Petit, Michel Polak, Krishna Chatterjee, Theo J Visser*, W Edward Visser

Summary

Background Deficiency of the thyroid hormone transporter monocarboxylate transporter 8 (MCT8) causes severe intellectual and motor disability and high serum tri-iodothyronine (T_3) concentrations (Allan–Herndon–Dudley syndrome). This chronic thyrotoxicosis leads to progressive deterioration in bodyweight, tachycardia, and muscle wasting, predisposing affected individuals to substantial morbidity and mortality. Treatment that safely alleviates peripheral thyrotoxicosis and reverses cerebral hypothyroidism is not yet available. We aimed to investigate the effects of treatment with the T_3 analogue Triac (3,3',5-tri-iodothyroacetic acid, or tiratricol), in patients with MCT8 deficiency.

Methods In this investigator-initiated, multicentre, open-label, single-arm, phase 2, pragmatic trial, we investigated the effectiveness and safety of oral Triac in male paediatric and adult patients with MCT8 deficiency in eight countries in Europe and one site in South Africa. Triac was administered in a predefined escalating dose schedule—after the initial dose of once-daily 350 µg Triac, the daily dose was increased progressively in 350 µg increments, with the goal of attaining serum total T_3 concentrations within the target range of 1·4–2·5 nmol/L. We assessed changes in several clinical and biochemical signs of hyperthyroidism between baseline and 12 months of treatment. The prespecified primary endpoint was the change in serum T_3 concentrations from baseline to month 12. The co-primary endpoints were changes in concentrations of serum thyroid-stimulating hormone (TSH), free and total thyroxine (T_4), and total reverse T_3 from baseline to month 12. These analyses were done in patients who received at least one dose of Triac and had at least one post-baseline evaluation of serum throid function. This trial is registered with ClinicalTrials.gov, number NCT02060474.

Findings Between Oct 15, 2014, and June 1, 2017, we screened 50 patients, all of whom were eligible. Of these patients, four (8%) patients decided not to participate because of travel commitments. 46 (92%) patients were therefore enrolled in the trial to receive Triac (median age 7·1 years [range 0·8–66·8]) . 45 (98%) participants received Triac and had at least one follow-up measurement of thyroid function and thus were included in the analyses of the primary endpoints. Of these 45 patients, five did not complete the trial (two patients withdrew [travel burden, severe pre-existing comorbidity], one was lost to follow-up, one developed of Graves disease, and one died of sepsis). Patients required a mean dose of 38.3 µg/kg of bodyweight (range 6·4–84·3) to attain T_3 concentrations within the target range. Serum T_3 concentration decreased from 4·97 nmol/L (SD 1·55) at baseline to 1·82 nmol/L (0·69) at month 12 (mean decrease 3·15 nmol/L, 95% CI 2·68–3·62; p<0·0001), while serum TSH concentrations decreased from 2·91 mU/L (SD 1·68) to 1·02 mU/L (1·14; mean decrease 1·89 mU/L, 1·39–2·39; p<0·0001) and serum free T_4 concentrations decreased from 9·5 pmol/L (SD 2·5) to 3·4 (1·6; mean decrease 6·1 pmol/L (5·4–6·8; p<0·0001). Additionally, serum total T_3 concentrations decreased by 31·6 nmol/L (28·0–35·2; p<0·0001) and reverse T_3 by 0·08 nmol/L (0·05–0·10; p<0·0001). Seven treatment-related adverse events (transiently increased perspiration or irritability) occurred in six (13%) patients. 26 serious adverse events that were considered unrelated to treatment occurred in 18 (39%) patients (mostly hospital admissions because of infections). One patient died from pulmonary sepsis leading to multi-organ failure, which was unrelated to Triac treatment.

Interpretation Key features of peripheral thyrotoxicosis were alleviated in paediatric and adult patients with MCT8 deficiency who were treated with Triac. Triac seems a reasonable treatment strategy to ameliorate the consequences of untreated peripheral thyrotoxicosis in patients with MCT8 deficiency.

Funding Dutch Scientific Organization, Sherman Foundation, NeMO Foundation, Wellcome Trust, UK National Institute for Health Research Cambridge Biomedical Centre, Toulouse University Hospital, and Una Vita Rara ONLUS.

Lancet Diabetes Endocrinol 2019
Published Online July 31, 2019 http://dx.doi.org/10.1016/S2213-8587(19)30155-X
See Online/Comment http://dx.doi.org/10.1016/S2213-8587(19)30217-7

*Dr Manshande died in August, 2018; Prof De Meirleir died in October, 2018; and Prof T J Visser died in March, 2018

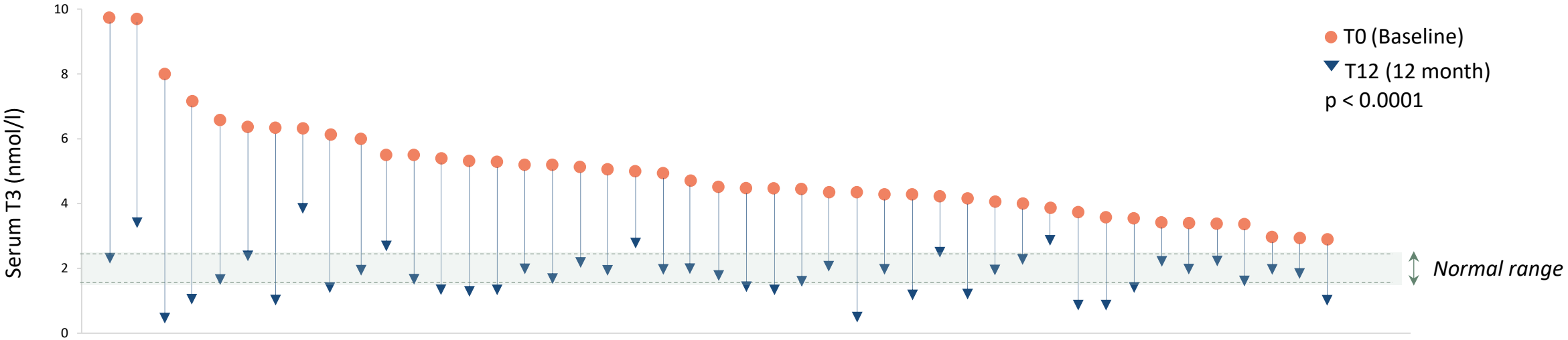
Academic Center for Thyroid Diseases (S Groeneweg MD, Prof R P Peeters MD, M Medici MD, Prof T J Visser PhD, W E Visser MD), Sophia Children's Hospital, Division of Paediatric Cardiology (J M van Beynum MD), Sophia Children's Hospital, Department of Paediatric Neurology (F M de Coo MD, F K Aansen PhD, M M van der Knoop MSc, M C Y de Wit MD), Department of Cardiology and Intensive Care Medicine (C A den Uil MD), Department of Clinical Chemistry (Prof Y B de Rijke PhD), and Department of Internal Medicine (Prof M C Zillikens MD), Erasmus Medical Centre, Rotterdam, Netherlands; Wellcome Trust-Medical Research Council Institute of Metabolic Science, University of Cambridge, Cambridge, UK (C Moran MB, A McGowan MD, G Lyons RCN, K Chatterjee FRCP); Paediatric Endocrinology, Diabetology and Gynaecology Department, Necker Children's University Hospital, Imagine Institute, Paris, France (A Stoupa MD, Prof M Polak M D); Department of Paediatric Endocrinology and Genetics, Children's Hospital, Toulouse University Hospital, Toulouse, France

Source: Groeneweg et al, Lancet D&E 2019;

© 2025 Egetis Therapeutics. All rights reserved.

Consistent, clinically relevant and highly significant results

Triac Trial I: Reached target level serum T3 & improvements in clinically relevant outcome measures

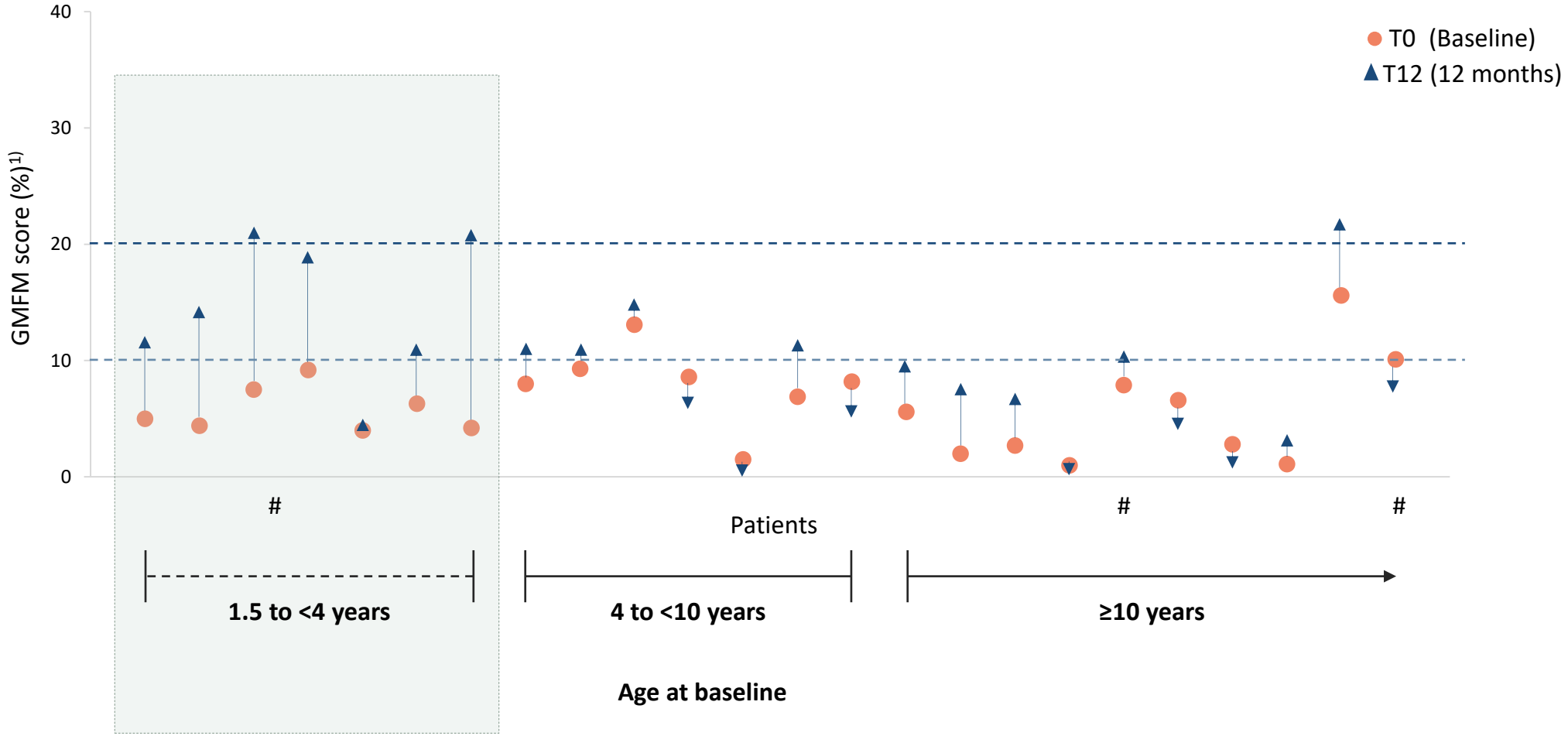


Endpoints	Baseline mean *(± SD)*	12 months mean *(± SD)*	Difference in means *(95% CI)*	p-value
Serum T3 (nmol/L)	4.97 (± 1.55)	1.82 (± 0.69)	-3.15 (-3.62, -2.68)	<0.0001
Weight for age (z score)	-2.98 *(± 1.93)*	-2.71 *(± 1.79)*	0.27 *(0.03, 0.50)*	0.025
Resting heart rate (bpm)	112 *(± 23)*	104 *(± 17)*	-9 *(-16, -2)*	0.01
Mean heart rate 24 h (bpm)	102 *(± 14)*	97 *(± 9)*	-5 *(-9, -1)*	0.012
SHBG (nmol/L)	212 *(± 91)*	178 *(± 76)*	-35 *(-55, -15)*	0.0013
Total cholesterol (mmol/L)	3.2 *(± 0.7)*	3.4 *(± 0.7)*	0.2 *(0.0, 0.3)*	0.056
CK (U/L)	108 *(± 90)*	161 *(± 117)*	53 *(27, 78)*	<0.0001

Source: Groeneweg et al; Lancet D&E 2019

Triac Trial I: Indication of positive effect on neurocognitive development

Triac Trial II did not meet its primary endpoints



Source: Groeneweg et al; Lancet D&E 2019

Real-world evidence: Long-term efficacy and safety of Emcitate® in MCT8 deficiency patients

Published in October, 2021

ACCEPTED MANUSCRIPT

Long-term efficacy of T3 analogue Triac in children and adults with MCT8 deficiency: a real-life retrospective cohort study

Ferdy S van Geest, Stefan Groeneweg, Erica L T van den Akker, Iuliu Bacos, Diana Barca, Sjoerd A A van den Berg, Enrico Bertini, Doris Brunner, Nicola Brunetti-Pierri, Marco Cappa ... Show more

Author Notes

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

- Investigator-initiated real-world cohort study at 33 sites conducted by the Erasmus Medical Center
- Investigated efficacy and safety of *Emcitate* in 67 patients with MCT8 deficiency
  - Median baseline age of 4.6 years (range: 0.5–66 years) and were treated with tiratricol for up to 6 years, with a median of 2.2 years (range 0.2 – 6.2 years)
  - The primary endpoint in the study was the change in serum T3 concentration from baseline to last-available measurement
  - The pre-specified secondary endpoints were key measurements of clinical complications of chronic peripheral thyrotoxicosis

New patient cohort of equal size to the Triac Trial I

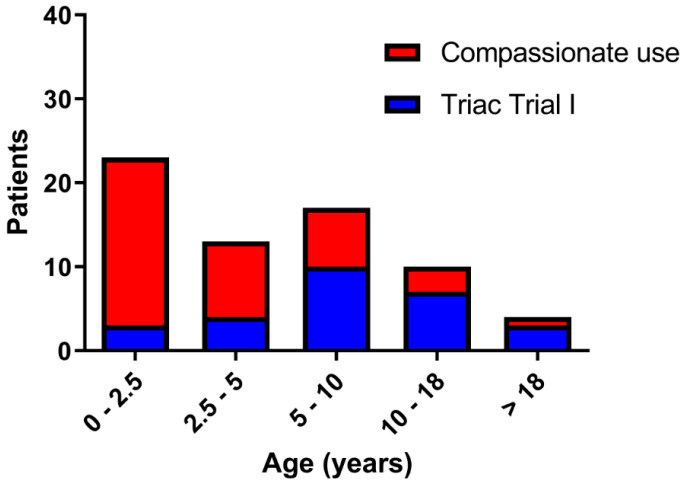
Long term follow up, up to >6 years

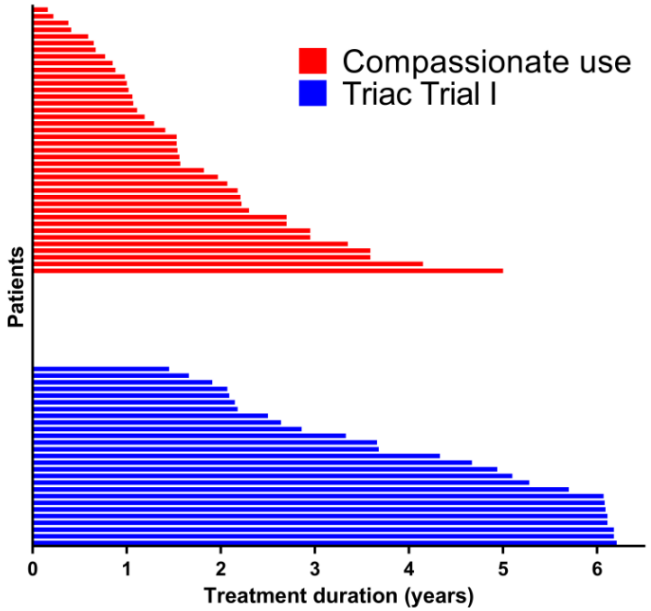
Triac Trial I
N=46

Triac Trial I patients
Available for long-term monitoring
N=27

New patients
From managed access program
N=40

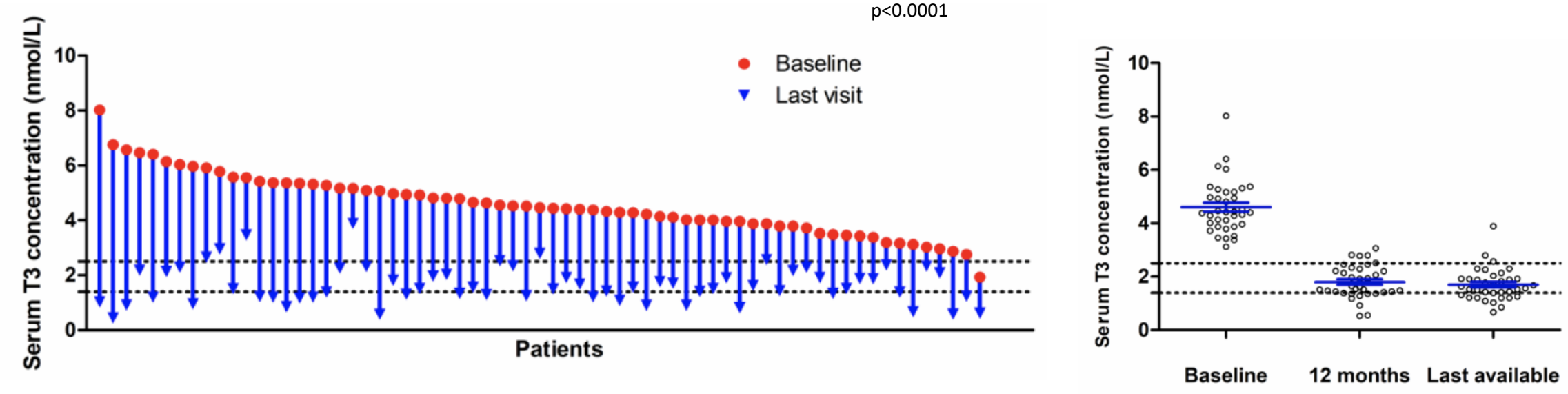
EMC cohort
Published in JCEM
N=67





New cohort confirms primary endpoint results in Triac Trial I

Fast and durable normalization of T3 values in almost all patients



Consistent, clinically relevant and highly significant results across endpoints

- Data confirm the positive results from previous study, Triac Trial I
- Normalization of serum T3 corresponds to improvement in thyroid hormone status in end target tissues
- Beneficial effects are maintained or continue to improve over time, up to six years
- Consistent efficacy seen across key clinical and biochemical parameters that were sustainably alleviated in patients with MCT8 deficiency regardless of age

Table 2: Changes from baseline to last visit in predefined outcomes

	Baseline mean (SD)	Last visit mean (SD)	Mean change (95% CI)	P value
Primary outcome				
T3 (nmol/L; n=67)	4.58 (1.11)	1.66 (0.69)	-2.92 (-3.23 to -2.61)	<0.0001
Secondary outcomes				
Anthropometric parameters and heart rate				
Body weight (kg; n=58)	17.8 (12.1)	23.6 (14.5)	5.7 (4.2 to 7.2)	
Weight-for-age Z score (n=58)	-2.81 (1.94)	-2.64 (1.81)	0.17 (-0.18 to 0.53)	0.3263
Δ Weight-for-age – predicted weight-for-age Z score (n=55)	0.07 (1.83)	0.79 (1.92)	0.72 (0.36 to 1.09)	0.0002
Height (cm; n=44)	101 (21)	116 (23)	15 (12 to 19)	
Height-for-age Z score (n=44)	-1.84 (1.77)	-1.92 (1.51)	-0.09 (-0.50 to 0.32)	0.6705
Δ Height-for-age – predicted height-for-age Z score (n=43)	-0.44 (1.38)	0.14 (1.41)	0.58 (0.12 to 1.05)	0.0139
Weight-for-height Z score (n=44)	-2.02 (2.49)	-1.50 (2.44)	0.52 (-0.35 to 1.39)	0.2358
Heart rate (bpm; n=48)	113 (21)	97 (20)	-17 (-24 to -10)	<0.0001
Heart rate-for-age Z score (n=48)	1.59 (0.89)	0.96 (1.01)	-0.64 (- 0.98 to -0.29)	0.0005
Thyroid function tests				
TSH (mU/L; n=62)*	3.32 (2.30)	0.95 (0.73)	-2.38 (-2.98 to -1.77)	<0.0001
Free T4 (pmol/L; n=64)	9.5 (2.3)	3.4 (1.6)	-6.1 (-6.7 to -5.4)	<0.0001
T4 (nmol/L; n=63)	54.2 (11.8)	18.1 (9.8)	-36.1 (-39.5 to -32.7)	<0.0001
Peripheral markers				
Sex hormone-binding globulin (nmol/L; n=48)	245 (99)	209 (92)	-36 (-57 to -16)	0.0008
Creatinine (µmol/L; n=47)	32 (11)	39 (13)	7 (6 to 9)	<0.0001
Creatine kinase (U/L; n=47)*	110 (87)	128 (80)	18 (-8 to 45)	0.2166
All outcomes were assessed in all patients who received Triac treatment longer than the mean time to optimal dose (5.0 months; N=64). Data are mean. Body weight-for-age Z scores were calculated using TNO growth calculator and heart rate-for-age Z scores were calculated using the Boston Z score calculator. Abbreviations: T3=tri-iodothyronine. TSH=thyroid-stimulating hormone. T4=thyroxine. *TSH and creatine kinase concentrations were log-transformed to ensure a normal distribution before paired t tests were done (non-transformed means [SDs] and mean changes [95% CIs] are presented for the sake of interpretability).				

Triac Trial II objective and design:

Triac Trial II was designed to investigate a potential additional benefit on neurocognitive development in 22 patients with MCT8 deficiency below 30 months of age treated with Emcitate® (tiratricol) during 96 weeks

Primary Objective	• Confirm findings from Triac Trial I in youngest age group • Improvement in neurocognitive development as measured by GMFM[1] and BSID-III[2] compared to natural history controls
Secondary Objective	• Achievement of motor milestones (e.g. hold head, sit independently) • Normalization of thyroid hormone function tests and markers of thyrotoxicosis
Description	• Open label, multi-centre trial in very young children with MCT8 deficiency • International trial with centres in CZ, DE, NL & US • Design discussed and anchored with EMA and FDA • ClinicalTrials.gov identifier: NCT02396459
# of Patients	• 22 children, 0-30 months of age
Timetable	• Topline 96-week results announced on June 19, 2024 • The trial did not meet its primary endpoints (please see next slide) • Market approval not dependent on Triac Trial II data

1. GMFM: Gross Motor Function Measure
2. BSID: Bayley Scales of Infant and Toddler Development

Triac Trial II Summary

- Triac Trial II results:
  - The numerical improvements versus baseline observed on the primary endpoints of neurocognitive development assessed by the GMFM-88 and BSID-III scales did not show a statistically significant improvement versus historical controls.
  - The trial confirmed the significant and durable reduction of T3 levels in all patients - relevant to alleviate features of thyrotoxicosis in patients with MCT8 deficiency.
  - Well-tolerated safety profile of tiratricol seen in previous clinical studies.
- The Triac trial II is complementary to the data already submitted and validated in the MAA for Emcitate® (tiratricol) for treatment of MCT8 deficiency, based on the benefit of normalization of thyrotoxicosis which has been demonstrated in patients of all ages, as agreed with the EMA. Results from Triac Trial II were included in the response to EMA 120-day list of questions in August 2024.
- The forthcoming NDA in the USA will also be based on the already observed treatment effects on T3 concentrations and the manifestations of chronic thyrotoxicosis together with results from the ongoing ReTRIACt trial, as acknowledged by the FDA.
- The timeline for regulatory review and approval in EU remain unchanged. For the US, as previously communicated, the Company will update the market with regards to timelines for NDA submission as soon as at least 16 evaluable patients have concluded the ongoing ReTRIACt trial.

Overview of changes in clinical variables during Triac Trial I

Real-world evidence: Tiratricol (Emcitate®) treatment in patients with MCT8 deficiency is associated with survival benefits

- Abstract published ahead of the ETA/ITC Annual Meeting report that treatment with tiratricol (Emcitate®) in patients with MCT8 deficiency is **associated with a 3x lower risk of mortality**.
- Retrospective real-world cohort study investigated the effects of tiratricol on mortality in 265 patients with MCT8 deficiency.

New data shows tiratricol (Emcitate®) treatment in patients with MCT8 deficiency is associated with survival benefits

August 21, 2024

- Abstract by F. van der Most et al. published ahead of the 46th Annual Meeting of the European Thyroid Association, to be held in Athens, Greece, on September 7-10, 2024.
- An international real-world cohort study included data from 228 patients collected from 173 sites in 48 countries.
- Treatment with the investigational drug tiratricol (Emcitate®) in pediatric and adult patients with MCT8 deficiency is associated with an approximately three times lower risk of mortality. This corroborates previous findings indicating that tiratricol sustainably alleviated key clinical features resulting from peripheral thyrotoxicosis.

Stockholm, Sweden, August 21, 2024. Egetis Therapeutics AB (publ) ("**Egetis**" or the "**Company**") (Nasdaq Stockholm: EGTX), today announced the content of an abstract by Dr Floor van der Most and co-authors, Erasmus Medical Center, Rotterdam, The Netherlands, published ahead of the 46th Annual Meeting of the European Thyroid Association, to be held in Athens, Greece, on September 7-10, 2024. In the Abstract, treatment with the investigational drug tiratricol (Emcitate®) in paediatric and adult patients with MCT8 deficiency is associated with an approximately three times lower risk of mortality compared to MCT8 deficiency patients not treated with tiratricol.

Post-hoc analysis reports effects of tiratricol on patient-centered outcome measures in patients with MCT8 deficiency

- According to the Abstract, there were improvements upon tiratricol treatment reported by caregivers related to improved interaction (22/39), greater alertness (19/39), improved motor skills (12/39), improved head control (7/39), and improved sleep (8/39).
- Compared to the baseline visit, excessive sweating was much less reported (48.6% vs. 8.1%) and less reduction in salivary flow was observed (30.6% vs. 22.2%) by the caregivers at the end study visit.
- **All parents (40/40)** preferred to continue tiratricol treatment.

New post-hoc analysis reports effects of tiratricol on patient-centered outcome measures in patients with MCT8 deficiency

August 28, 2024

- An Abstract by Dr M. Freund and co-authors from Erasmus Medical Center, Rotterdam, The Netherlands, published ahead of the Annual Meeting of the European Thyroid Association reports that treatment with the investigational drug tiratricol exerts beneficial effects on several patient-centered outcome measures in MCT8 deficiency.

Stockholm, Sweden, August 28, 2024. Egetis Therapeutics AB (publ) ("**Egetis**" or the "**Company**") (Nasdaq Stockholm: EGTX), today announced the content of an Abstract by Matthijs Freund and co-authors, Erasmus Medical Center, Rotterdam, The Netherlands, published ahead of the 46th Annual Meeting of the European Thyroid Association, to be held in Athens, Greece, on September 7-10, 2024. In this analysis the authors performed post-hoc analyses on caregiver-reported patient-centered outcome measures in the Triac Trial I (1). In this trial, 40 patients with MCT8 deficiency completed 1 year of tiratricol treatment. At baseline, during clinical visits and at the end of the study, semi-structured interviews were held with caregivers on complex needs and daily care challenges, including motor skills, sleep problems, and seizure frequency. Moreover, parents were asked to report perceived changes in (thyrotoxic) symptoms such as increased sweating and reduction in salivary flow.

Appendix 3

Emcitate® - regulatory pathways in EU and US

Regulatory features of *Emcitate* for MCT8 deficiency

ODD

Orphan drug designation for MCT8 deficiency
Eligibility: Market exclusivity 10y (EU) & 7y (US)

BTD

Breakthrough Therapy Designation (FDA)

PRV

Rare pediatric disease designation (FDA)
Eligibility: Priority review voucher upon approval*

MAA
NDA

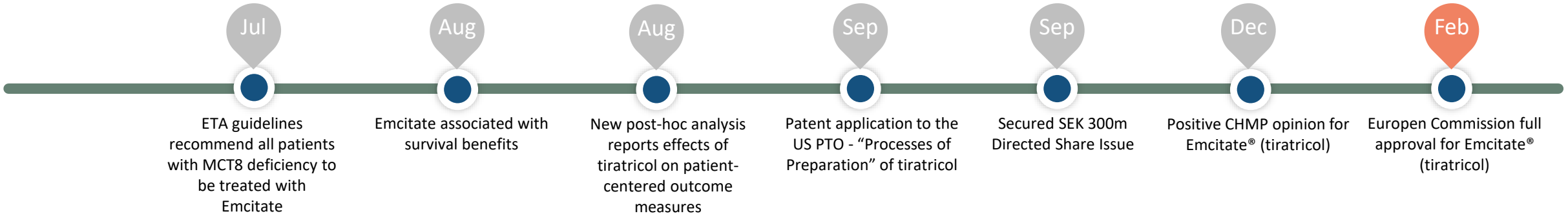
MAA: EU full approval received in February 2025
NDA: Ongoing ReTRIACt withdrawal study

ODD

Orphan drug designation for RTH-beta

*The voucher may be sold to another sponsor (2023-25 range: ~$100m-$158m)

EU Commission approves Emcitate® as the first and only treatment for patients with MCT8 deficiency



- **Full marketing authorisation**.

"This is the single most important milestone in Egetis' history and a major step forward in building a sustainable rare disease company"

PRESS

European Commission approves Egetis' Emcitate® (tiratricol) as the first and only treatment for patients with MCT8 deficiency

February 13, 2025

Stockholm, Sweden, February 13, 2025. Egetis Therapeutics AB (publ) ("Egetis" or the "Company") (Nasdaq Stockholm: EGTX), today announced that the European Commission (EC) has approved Emcitate® (tiratricol) for the treatment of patients with monocarboxylate transporter 8 (MCT8) deficiency. Emcitate is the first and only medicine authorised in the EU to treat MCT8 deficiency. The full indication is: Emcitate is indicated for the treatment of peripheral thyrotoxicosis in patients with monocarboxylate transporter 8 (MCT8) deficiency (Allan-Herndon-Dudley Syndrome), from birth.

Nicklas Westerholm, CEO of Egetis, commented: *"We are proud of the European Commission approval of Emcitate, which marks the first and only approved treatment for patients with MCT8 deficiency. This approval represents the single most important milestone in Egetis' history and a major step forward in building a sustainable rare disease company. We are delighted to bring this much needed new treatment to patients.*

"I would like to thank all patients, parents, caregivers and investigators who have taken part in the comprehensive development program for Emcitate and all Egetis employees and collaborators for their dedicated and hard work, in particular the group of Prof. Dr. Edward Visser at the Erasmus University Medical Center, Rotterdam, The Netherlands.

"We look forward to initiating pricing and reimbursement processes and discussions in Europe and expect the first launch in the second quarter of 2025."

Emcitate/tiratricol regulatory pathway in EU/US

Robust data set in an ultra rare genetic disease

Triac Trial I	EMC cohort study	Natural history	Triac Trial II	EMC survival study	ReTRIACt
N=46	N=67	N=151	N=22	N>600	N=15
• Completed 2018 (Groeneweg, 2019) • Open-label, international, multi-centre study	• Completed 2021 (van Geest, 2022) • N= 27 from Triac Trial I & N= 40 new pts from managed access program	• Retrospective data, 2003 to 2019 (Groeneweg, 2020)	• Open-label, international, multi-centre study • Focus on neurocognition; did not meet its primary endpoints • 96 weeks safety data in young patients	• Basis for Breakthrough Therapy Designation by FDA • Comparing treated vs untreated patients on survival • Treatment with tiratricol (Emcitate®) is **associated with a 3x lower risk of mortality**	• Placebo-controlled withdrawal study • SAP revised • Topline results expected Q4 2025

Data included in EMA MAA – EC approval Feb 2025

Data to be included in FDA NDA

EMC: Erasmus Medical Center; SAP: Statistical Analysis Plan

ReTRIACt: withdrawal of *Emcitate* in males with MCT8 Deficiency

Randomized placebo-controlled trial: complementary for NDA submission

Primary endpoint

Oct. 23, 2025: FDA has recommended that the Statistical Analysis Plan (SAP) for the ReTRIACt trial will be revised and the study will be closed. Topline results will be communicated during the fourth quarter of 2025. Data accrued to date will be included in the NDA.

Secondary endpoints

Description

- Double-blind, randomized, multicenter placebo-controlled study
- Participants with stable maintenance treatment with *Emcitate* or treatment-naïve patients
- Clinicaltrials.gov identifier: NCT05579327

# of patients

- 15 evaluable patients, > 4 years of age
- Patients from Managed Access program and treatment naïve patients

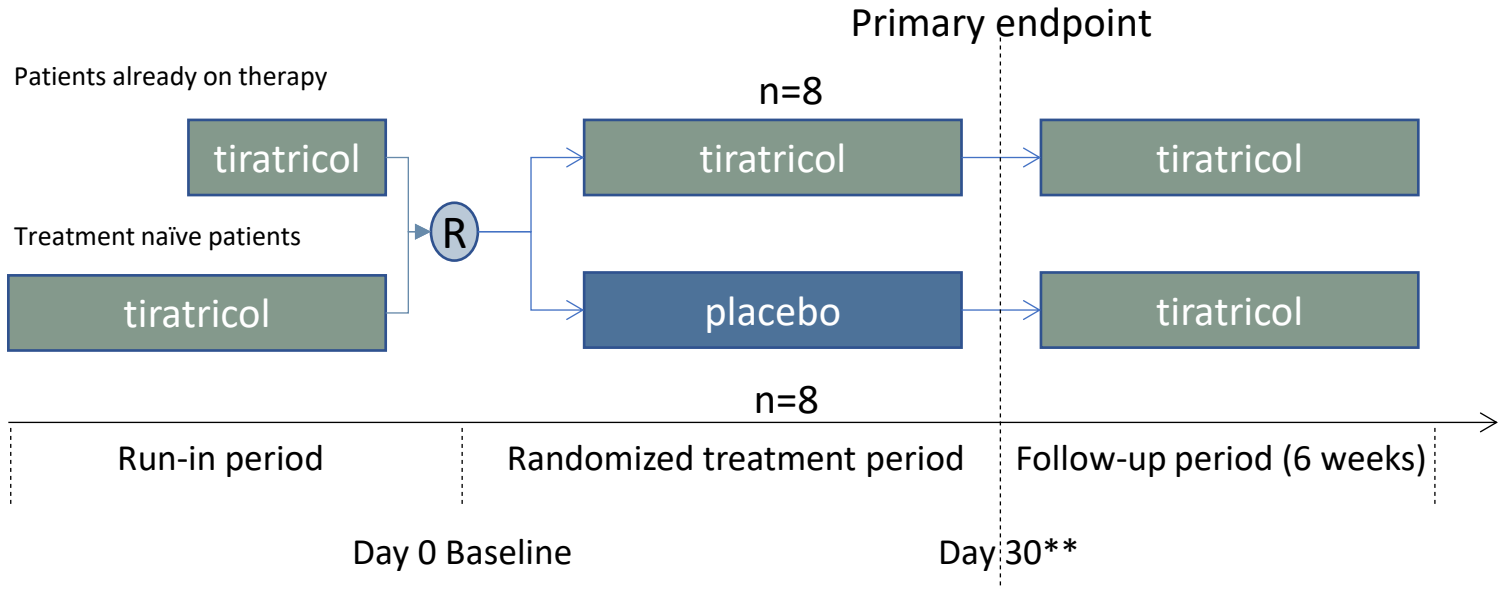
Timetable

- First patients recruited Q3 2023
- Topline results expected Q4 2025

Design of the ReTRIACt trial (status October 23, 2025)

Requested by and agreed with the FDA

- A 30-day, randomized placebo-controlled withdrawal study in 15 patients
- The study allowed for inclusion of patients that were already on therapy and patients that were treatment naïve
- Treatment naïve patients require a longer run-in period to stabilize T3 levels around normal range before randomization



- There are 15 evaluable patients in the ReTRIACt trial
- As recommended by the FDA, the Statistical Analysis Plan for the ReTRIACt trial will be revised and the study will be closed
- Complementary study to the survival data and other clinical components in the NDA
- Topline results expected in the fourth quarter of 2025. Data accrued to date will be included in the NDA

Initiation of rolling NDA submission planned in December 2025, with NDA completion early 2026

BTD: Breakthrough Therapy Designation

Value enhancing key milestones 2025-2026

Emcitate® — **2025-2026**

MCT8 deficiency

- ✓ EU launch, in the first country, Germany, May 1, 2025
- ✓ Break Through Designation granted by FDA
- ✓ Türkiye partnership signed with Er-Kim
- Topline results ReTRIACt
- Submission of US NDA – priority review
- Middle East, North Africa partnership/s
- Japan – Development plan agreed with PMDA
- US Patent granted - Processes and compounds
- US approval and launch
- US Rare Pediatric Disease Priority Review Voucher

RTH-beta

- Potential initiation of Investigator Initiated Study - Egetis Industry collaborator

Appendix 4

Emcitate® - Commercial opportunity

Emcitate®– alleviating patient and societal burden

Aiming to provide value for both patients and society

MCT8 deficiency is a detrimental condition with significant unmet medical need and no approved therapy

Patients

- Median life-expectancy of MCT8 patients is 35 years[1]
- Patients underweight for age or without ability to hold head have an even increased risk of premature death

Society

- All MCT8 patients have significant neurocognitive disability from early childhood and typically require constant, life-long supportive care
- A recent study in a condition with similar severity (SMA) estimated total healthcare cost (excluding treatment cost) to USD 138k per patient and year[2]

Emcitate holds potential to become the **first approved therapy** to address the root cause of MCT8 deficiency, restore thyroid hormone signaling and thereby **prevent disease progression**, alleviate symptoms and **prolong lives**

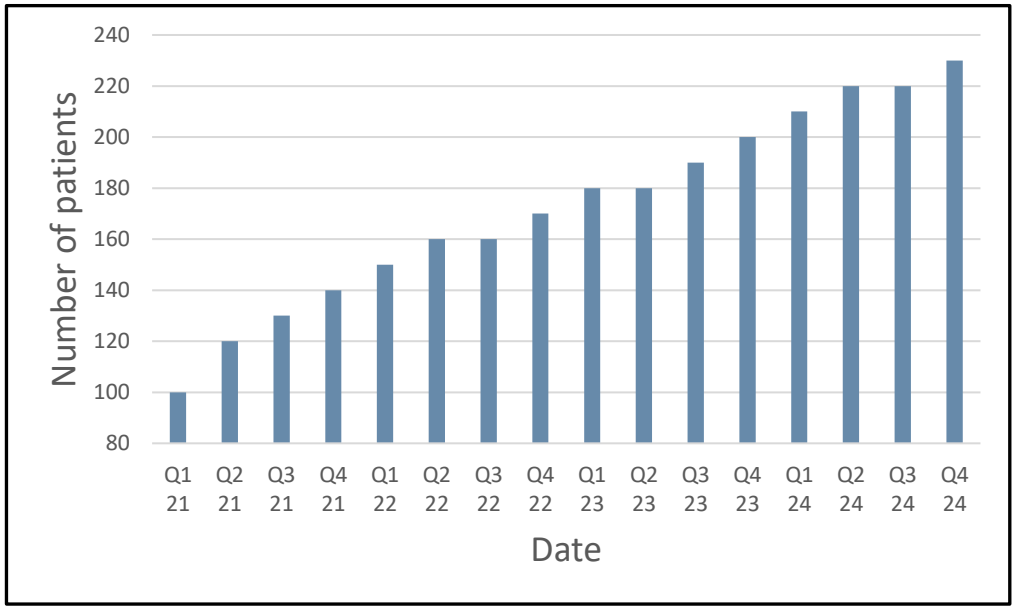
Source: (1) Disease characteristics of MCT8 deficiency: an international, retrospective, multicentre cohort study, Groeneweg et al, The Lancet, 2012; (2) Economic burden of spinal muscular atrophy in the United States: a contemporary assessment, Droege et al, Journal of Medical Economics, 2020;

Tiratricol supplied globally in managed access programs

Managed access programs confirm the significant unmet medical need in MCT8 deficiency

- Managed access programs
  - mechanisms to allow early access to a medicine prior to regulatory marketing approval
  - granted to pharmaceuticals under development for situations with high unmet medical needs and where no available treatment alternatives exist or are suitable
- FDA approved Expanded Access Program - Simplifies Process for Accessing tiratricol
- Tiratricol is being supplied in managed access programs, following individual approval from the national medicines agencies, to
  - Over 230 patients (at end Q1 2025)
  - Over 25 countries

Patients Receiving Emcitate in Managed Access Programs



Commercialization possible with lean & agile team

Unique setting for Emcitate in MCT8 deficiency

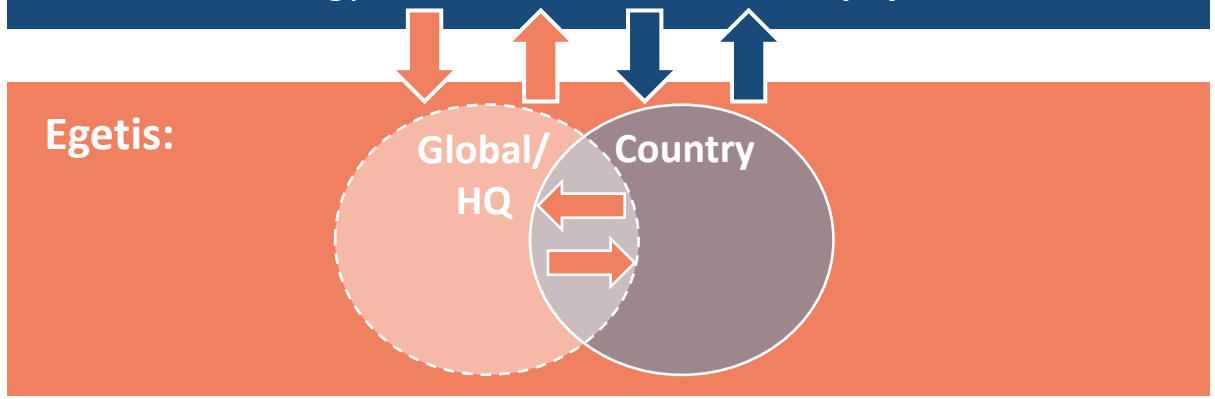
- Addressing unmet medical need
- No competition
- KOL support
- Centralized care guidance
- Global community

Seizing opportunity for cost-effective value creation

- Targeted stakeholder interactions
- Efficiency gains through global-country team coordination

External Key Stakeholders:

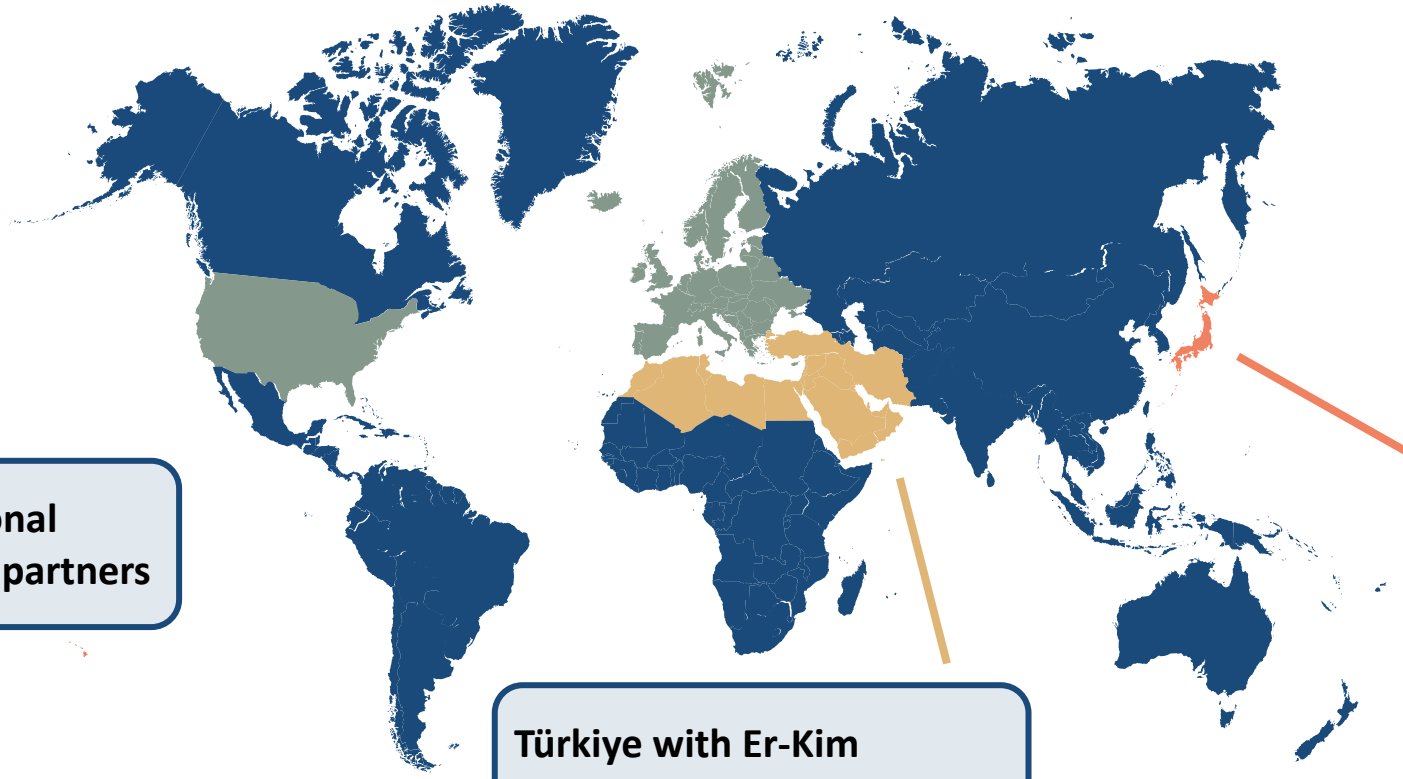
- **Caregivers** connected through international & national advocacy groups
- International **KOLs** & **physicians** at selected specialist centers
- Global strategy and local interactions with **payers**



Emcitate launch by Egetis and partners

Executing the US & European market preparations and launches through the Egetis team

To optimize the launch, we will focus our own resources on US and Europe (> 70% of sales for most ultra-orphans)



Optimizing additional countries through partners

Türkiye with Er-Kim MENA partnering dialogues

Japan license deal with Fujimoto

Step-wise building team to execute on key activities at the right time for launch success

Key projects driven by recognized industry talents recruited to the Egetis Commercial & Medical Affairs Team

– Core team brings launch skills and best practices from in total 150+ years at international companies

Henrik Krook, SE
VP, Commercial Operations

ALEXION

Henna Oittinen Corbinelli, CH
Medical Director Europe & International

BAYER

Nadia Georges, CH
Global Head, Market Access & Pricing

SANOFI

Azza Trad, FR
GM France

sobi
Pioneer in Rare Diseases

Peter Verwaijen, NL
Global Head Brand Strategy & Commercial Business Expansion, GM Benelux

ACTELION

Anny Bedard, US
President Egetis North America

Shire

Ann-Marie Redmond, US
Head of Market Access & Pricing, North America

Otsuka

Karen Anderson, US
Head of Medical Affairs, North America

agios

Nigel Nicholls, UK
Global Patient Advocacy Director & GM UK, Northern Europe & Iberia

BIOMARIN

Raymond Francot, NL
GM for DACH, IT, Central & Eastern Europe

VERTEX

Focusing on Critical Areas for Launch Success

Aiming to Improve the Lives of MCT8 Deficiency Patients and their Caregivers

IDENTIFY PATIENTS

Boost disease awareness, educate on disease*, diagnosis and newborn screening

ENSURE ACCESS

Preparing for broad access to Emcitate as soon as possible after marketing authorization

*Emcitate promotion will start at the time of marketing authorization (in line with legislations). Before that, external initiatives are focused on MCT8 deficiency.

Expanding disease awareness momentum

Amplified by External Efforts

Constructive dialogues at scientific congresses

Scientific community generating more data

Example from Annual Meeting of the European Thyroid Association

Van der Most, F. et al. T3 analogue Triiodothyroacetic acid (Triac) treatment and survival in MCT8 deficiency: an international real-world cohort study

Freund, M. et al. Effect of the T3 analogue Triac on patient-centered outcome measures in patients with MCT8 deficiency: post-hoc analysis of the international Triac Trial I

5 additional abstracts related to MCT8 deficiency

Great work ongoing by several patient advocacy groups

MCT8 - AHDS Foundation

MCT8 Forschung e.V.

SHERMAN FOUNDATION

EURORDIS RARE DISEASES EUROPE

Thyroid Federation International

European Reference Networks #ERNcare4Us Rare Diseases Doctors

NORD National Organization for Rare Disorders

Xtraordinaire.org Handicaps mentaux liés au chromosome X Association de familles

Deliver solid *Emcitate* clinical and economic value proposition to enable reimbursement & broad access

Key for payer assessments to describe burden of disease, unmet need & benefit of treatment

High burden of MCT8 deficiency

Recently further supported by Egetis sponsored Caregiver study*


Caregiver-reported quality of life of patients with MCT8 deficiency: Results from a cross-sectional survey


Quality of Life Impact of Caregiving for Patients with MCT8 Deficiency: Results From a Cross-Sectional Survey

Significant unmet medical need

Currently no drug developed and regulatory approved for MCT8 deficiency

Emcitate benefit validated by physicians and regulators

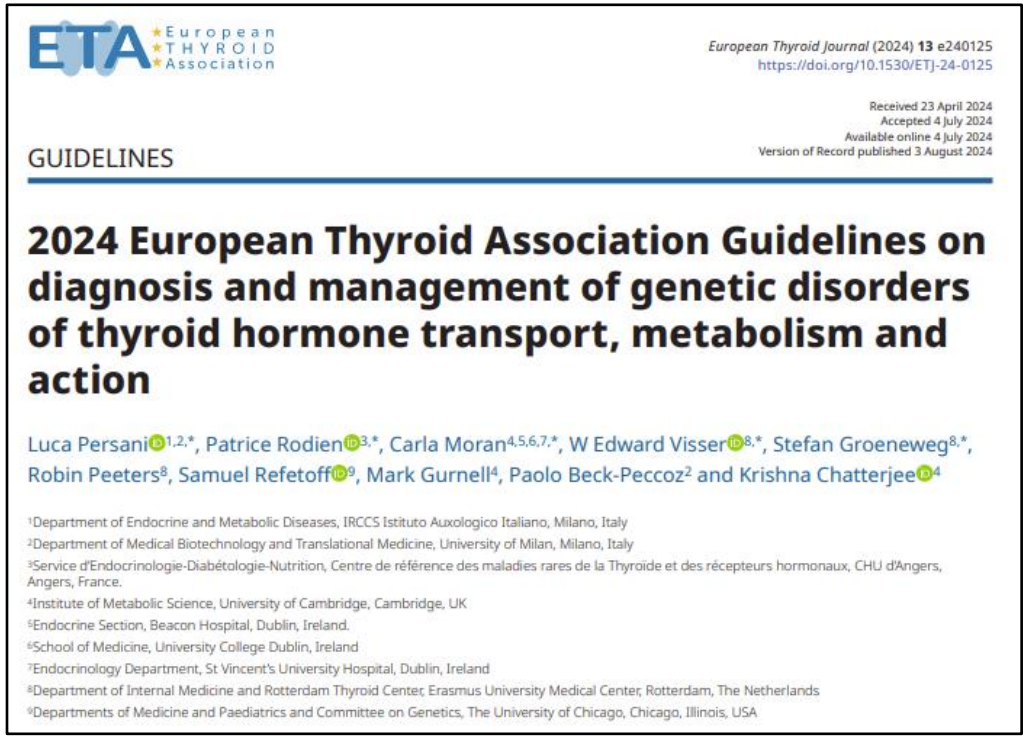
The existing clinical experience and data contributed to:

- European Thyroid Association (ETA) recommending Emcitate as long-term therapy for all patients with MCT8 deficiency
- Positive CHMP opinion

* Posters presented at congresses 2024, at ESPE (European Society of Pediatric Endocrinology) and ISPOR (International Society for Pharmacoeconomics and Outcomes Research).

European Thyroid Association (ETA) recommends tiratricol as long-term therapy for all patients with MCT8 deficiency

- ETA recommends the **use of tiratricol as long-term therapy for all patients** with MCT8 deficiency, and for certain patients with RTH-beta.
- Inaugural 2024 Guidelines were commissioned by the Executive Committee of the ETA and developed by an independent team of experts.



ETA European THYROID Association

European Thyroid Journal (2024) **13** e240125
https://doi.org/10.1530/ETJ-24-0125

Received 23 April 2024
Accepted 4 July 2024
Available online 4 July 2024
Version of Record published 3 August 2024

GUIDELINES

2024 European Thyroid Association Guidelines on diagnosis and management of genetic disorders of thyroid hormone transport, metabolism and action

Luca Persani[1,2,*], Patrice Rodien[3,*], Carla Moran[4,5,6,7,*], W Edward Visser[8,*], Stefan Groeneweg[8,*], Robin Peeters[8], Samuel Refetoff[9], Mark Gurnell[4], Paolo Beck-Peccoz[2] and Krishna Chatterjee[4]

[1]Department of Endocrine and Metabolic Diseases, IRCCS Istituto Auxologico Italiano, Milano, Italy
[2]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milano, Italy
[3]Service d'Endocrinologie-Diabétologie-Nutrition, Centre de référence des maladies rares de la Thyroïde et des récepteurs hormonaux, CHU d'Angers, Angers, France.
[4]Institute of Metabolic Science, University of Cambridge, Cambridge, UK
[5]Endocrine Section, Beacon Hospital, Dublin, Ireland.
[6]School of Medicine, University College Dublin, Ireland
[7]Endocrinology Department, St Vincent's University Hospital, Dublin, Ireland
[8]Department of Internal Medicine and Rotterdam Thyroid Center, Erasmus University Medical Center, Rotterdam, The Netherlands
[9]Departments of Medicine and Paediatrics and Committee on Genetics, The University of Chicago, Chicago, Illinois, USA

A phased EU launch through in-house commercial organization starting in Germany May 1

Pricing & Reimbursement (P&R) strategy execution in 2 waves, starting with EU4

Wave 1

France, Germany, Italy, Spain

Wave 2

Phased on a country-by-country approach

Rest of Europe

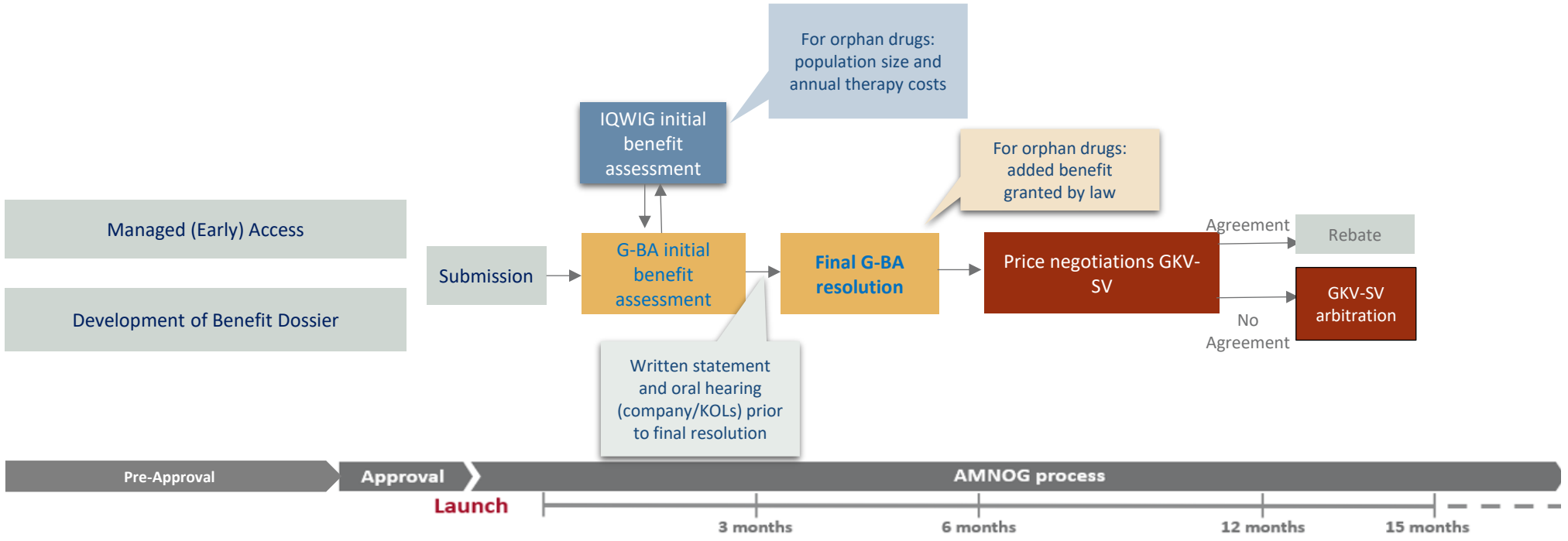
Pricing & Reimbursement processes

Deliver the *Emcitate* clinical and economic value proposition in P&R processes, outlining:

- MCT8 deficiency and its rarity
  - Summarizing available literature
- High burden of MCT8 deficiency
  - Confirmed by Egetis sponsored Caregiver study
- Significant unmet medical need
  - Emcitate the first & only approved treatment
- Benefit of treatment
  - Supported by publications & ETA guidelines

Germany: Benefit assessment and price negotiations for new drugs follow a strict and transparent process

AMNOG Process is well-defined and led by G-BA for benefit assessment and by GKV for price negotiations



4 parties involved in AMNOG process:

EGETIS THERAPEUTICS

Gemeinsamer Bundesausschuss

IQWiG

GKV

G-BA: Gemeinsamer Bundesausschuß - Federal Joint Commission
GKV-SV: Gesetzliche Krankenversicherung Spitzenverband - Statutory Health Insurance
IQWiG: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen – Institute for quality and Efficiency in Health Care
KOLs: Key Opinion Leaders

Germany Launch Strategy

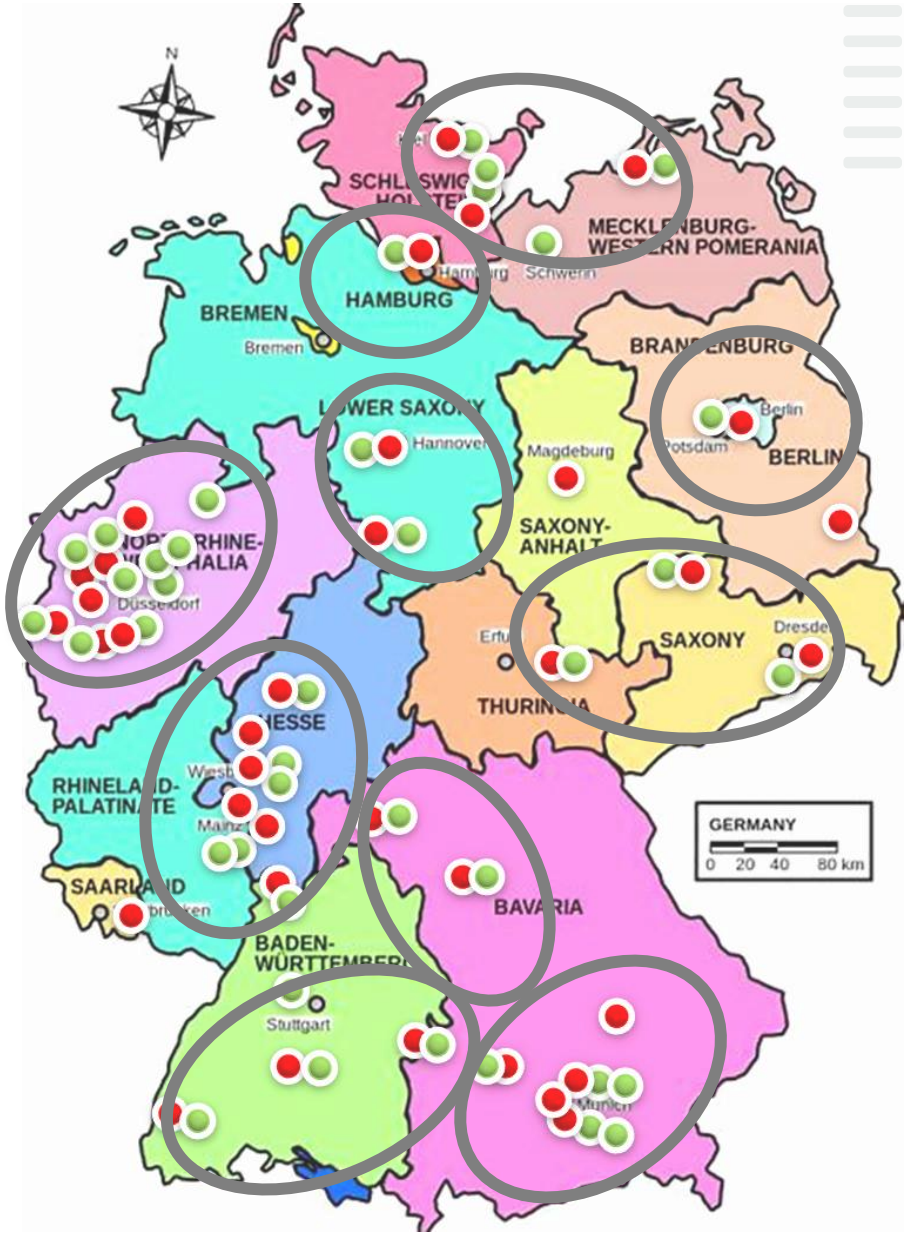
Building strong Expert base to advance management of MCT8 deficiency

MCT8 deficiency Experts

- Engage experts in increasing disease awareness in Germany
- Advance collaborative efforts on monitoring and treatment guidance of MCT8 deficiency
- Advocate for importance of local publications & clinical training in managing MCT8 deficiency

HCPs involved in patient journey

- Collaborate with SPZs and ZSEs involved in MCT8 deficiency patient journey and subsequent disease management
- Increase disease awareness and encourage discussions in local educational training sessions in multidisciplinary HCP teams
- Develop customized awareness campaigns to HCPs as well as patient support materials in collaboration with disease experts



IIS: Investigator Initiated Studies
SPZs: Sozialpädiatrische Zentren – Social Pediatric Centers
ZSEs: Zentren für Seltene Erkrankungen – Centers for Rare Diseases

Entering new phase with EU approval and Germany launch

As of May 1: Easier access to Emcitate and promoting Emcitate e.g. at congresses

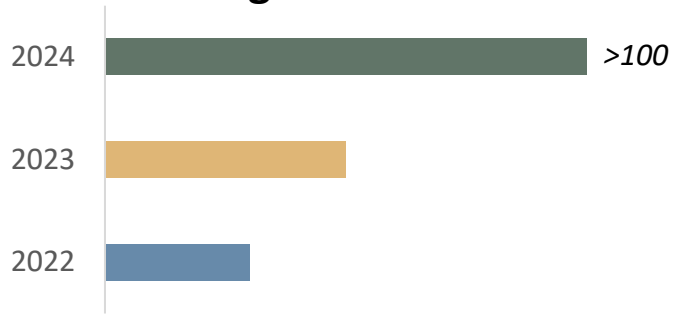
Congresses, H1	Geogr. scope	When
APS	Germany	March √
Deutsche Gesellschaft für Endokrinologie (DGE)	Germany	March √
DACH Kongress für seltene Erkrankungen	DACH	April √
APEDÖ	DACH	April √
Joint Congress of ESPE and ESE 2025	Europe	May √
Luisenthaler Gespräche (Endocrinology)	Germany	May √

For analysts and investors

US commercial preparedness activities under way

Accelerate patient finding efforts by integrating advanced data-driven insights into existing initiatives

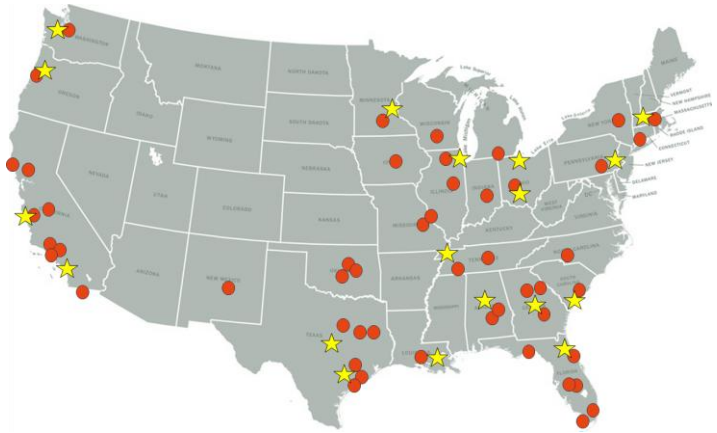
Known confirmed diagnosed MCT8 deficiency patients in the US



Naive or treated under early access

Cover major US centers through pre-commercial initiatives

- Hospitals with known MCT8 deficiency patients
- ★ *Tiratricol* Expanded Access Program sites, active & in process



Expanded Access Program, requested by FDA, is a significant asset to both patients and Egetis launch readiness

- Providing early and sustainable access to therapy
- Physicians gain experience of tiratricol
- Opportunity to generate real world data to support regulatory and payer interactions

Patient-centric implementation

- Partnership with AnovoRx
- Personalized support; drug delivered directly to patient home

Disclaimer: tiratricol is investigational and has not been approved by the U.S. Food and Drug Administration (FDA). Its safety and efficacy have not been established for the US market.

Balancing Annual Treatment Costs and Broad Access

Analogues

Product	Disease	Estimated annual treatment cost (WAC)
Skyclarys® *Small molecule*	Friedreich ataxia	~$400K
Procysbi® *Small molecule*	Nephropathic cystinosis	~$550K
Ravicti® *Small molecule*	Urea cycle disorder	~$750K
Exondys® *Antisense oligonucleotide*	Duchenne Muscular Dystrophy	~$750K

Access

Less restrictive
- Prior Authorization to label
- Genetic Test Attestation/documentation
- Specialist prescribing

More restrictive
- Prior Authorization beyond label
- Attestation of clinical benefit
- Medical exception with appeal

Appendix 5

Emcitate partnerships

Advancing rest of world with license agreement with Fujimoto for Emcitate in Japan

- **Highly suitable partner in Fujimoto**
  - Private company in Osaka, Japan, founded in 1933
  - Significant experience from successfully registering and launching medicines for Blood, Neurological and Orphan diseases in Japan
- **Egetis retains significant share of future revenues in Japan**
  - Upfront, development & regulatory milestones of total JPY 600m (SEK 45m)
  - In addition, Fujimoto will finance the necessary development in Japan and be responsible for regulatory interactions
  - Egetis retains ~1/3 of future revenues

Egetis announces exclusive license agreement with Fujimoto to develop and commercialize Emcitate in Japan

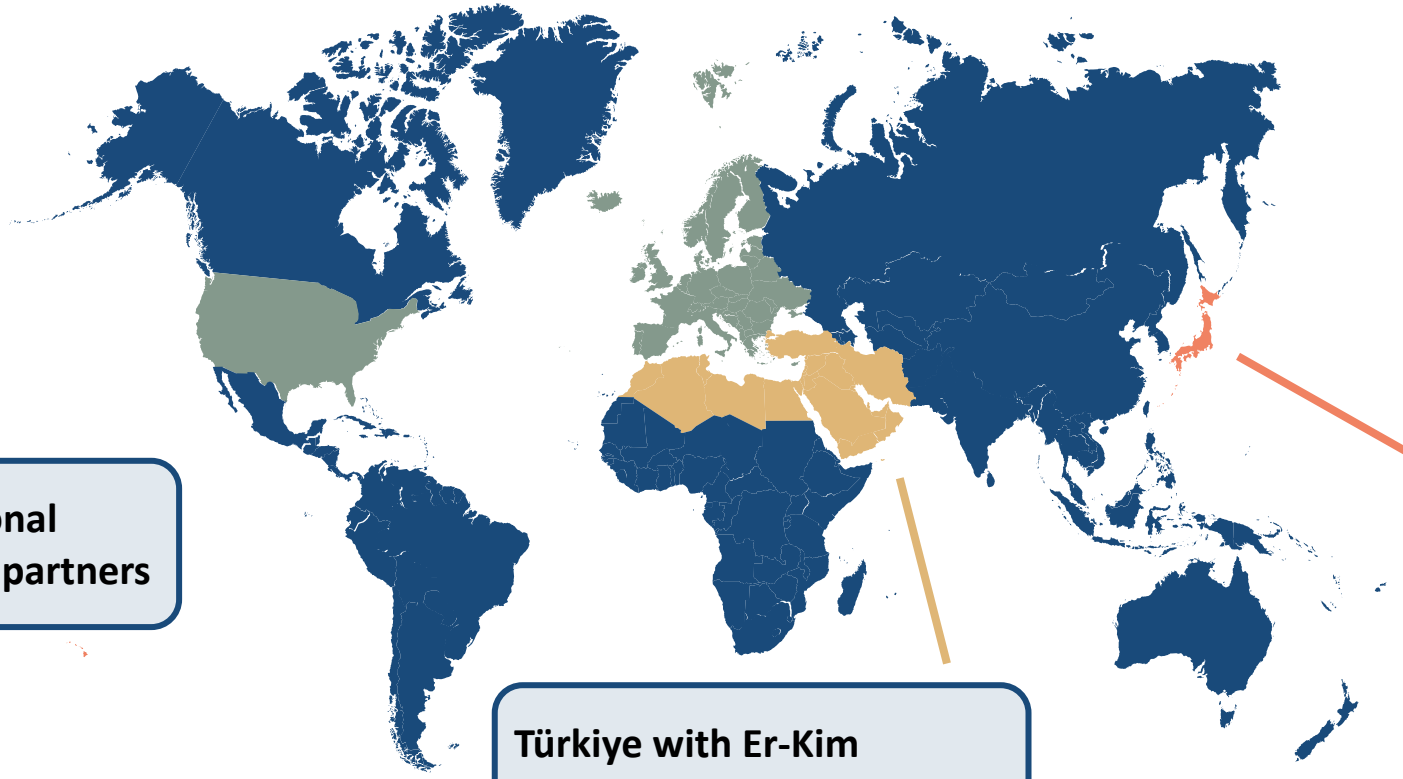
November 10, 2023

Stockholm, Sweden, November 10, 2023. Egetis Therapeutics AB (publ) ("**Egetis**" or the "**Company**") (Nasdaq Stockholm: EGTX), today announced that the Company, through its wholly-owned subsidiary Rare Thyroid Therapeutics International AB, has entered into an exclusive license agreement with Fujimoto Pharmaceutical Corporation ("**Fujimoto**") to develop and commercialize *Emcitate* (tiratricol), for the treatment of MCT8 deficiency, in Japan. Under the terms of the agreement Egetis grants Fujimoto exclusive development and commercialization rights to *Emcitate* for the treatment of MCT8 deficiency in Japan. Fujimoto will pay upfront, development, and regulatory milestones amounting to JPY 600 million (approximately SEK 45 million). Egetis will supply Fujimoto with product in semi-finished form and will receive approximately one third of the applicable income from Fujimoto. Fujimoto will also finance the development program needed for *Emcitate* in Japan, which will be clarified after discussions with the Pharmaceuticals and Medical Devices Agency (PMDA). As a future marketing authorisation holder (MAH) Fujimoto will be responsible for regulatory interactions with the PMDA.

Emcitate launch by Egetis and partners

Executing the US & European market preparations and launches through the Egetis team

To optimize the launch, we will focus our own resources on US and Europe (> 70% of sales for most ultra-orphans)



Optimizing additional countries through partners

Türkiye with Er-Kim MENA partnering dialogues

Japan license deal with Fujimoto

Appendix 6

Potential for indication expansion into RTH-beta

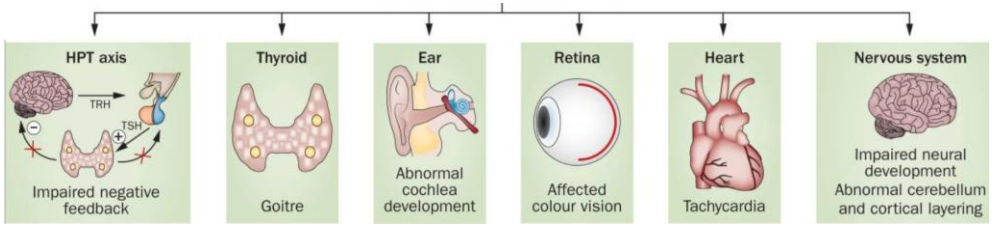
Resistance to Thyroid Hormone type Beta (RTH-β)

Potential indication expansion for Emcitate into non-overlapping patient population

Characteristics of RTH-β

- Caused by mutations in thyroid hormone receptor beta (TRβ)[1]
- Reduced target tissue response to thyroid hormone in TRβ dependent tissues
- Incidence 1:20,000 to 1:40,000 (both genders)
- Clinical heterogeneity, ranging from mild to severe
- Diagnosis: High T3&T4, normal/high TSH; confirmed by sequencing of the TRβ gene
- Clinical phenotypes: goiter, CV issues, failure to thrive, neurocognitive dysfunction

Overview of tissues affected in RTH-β



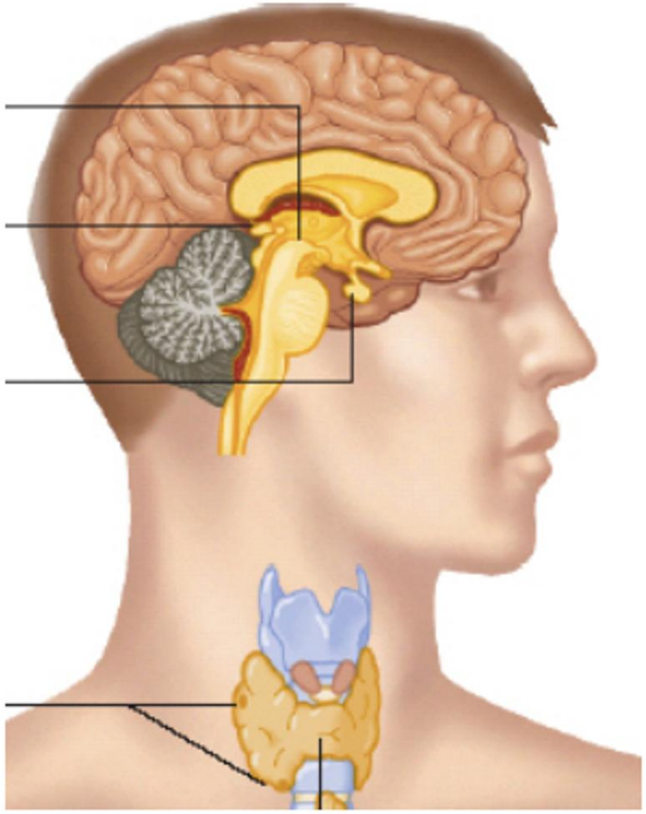
Emcitate as potential treatment for RTH-β

- *Emcitate* efficacious in restoring signaling in majority of TRβ mutations *in vitro*
- Initial clinical experience demonstrates positive effects on key clinical symptoms in RTH-β patients, including cardiovascular, thyrotoxic and neuropsychiatric symptoms[2]
- Mechanistic rationale: *Emcitate* has a higher affinity than T3 for several TRβ-mutants identified
- *Emcitate* received orphan drug designation for RTH-β from FDA and EMA in 2022
- Development plan for *Emcitate* in RTH-β under evaluation

References:

1. Pappa & Refetoff (2021) Front. Endocrinol. 12, 656551
2. Anzai et al. (2012) Thyroid 22, 1069-1075

“The Feedback Loop” in RTHβ



Pituitary

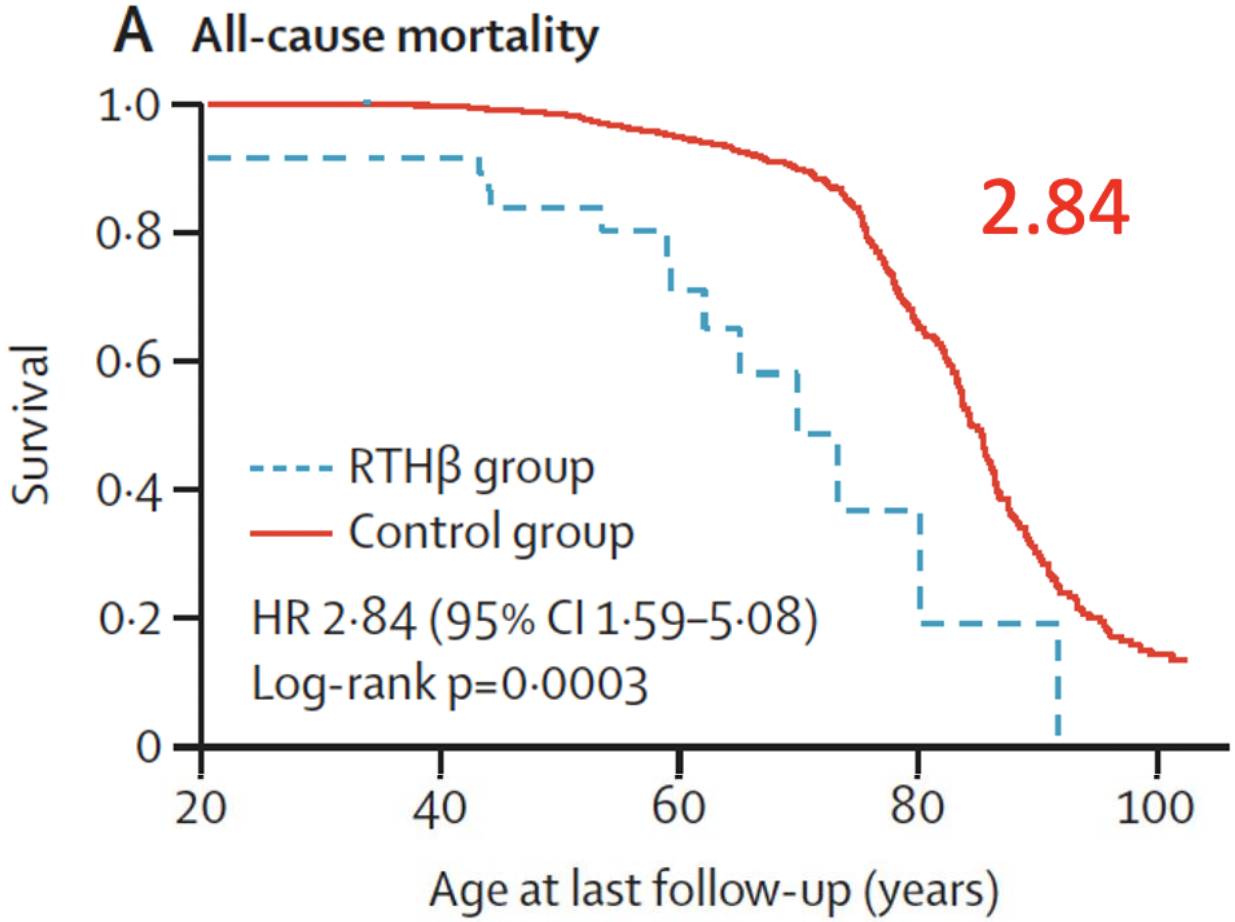
Thyroid

Thyroid Stimulating Hormone (TSH)

Thyroid Hormones
T4 and T3

		Example levels	Normal Levels
TSH	NORMAL RANGE	4.0	0.27-4.2
T4	HIGH	45	12-22
T3	HIGH	22	3.1-6.8

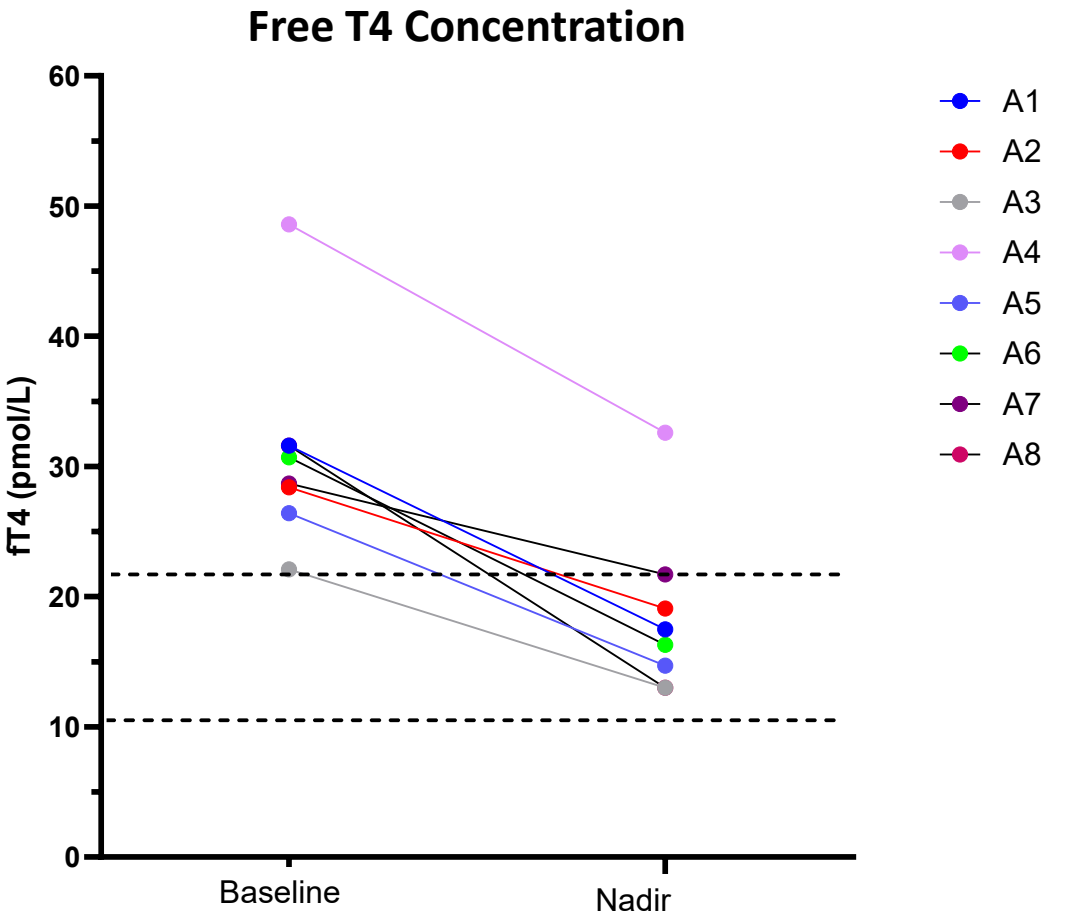
Increased Mortality RTHβ

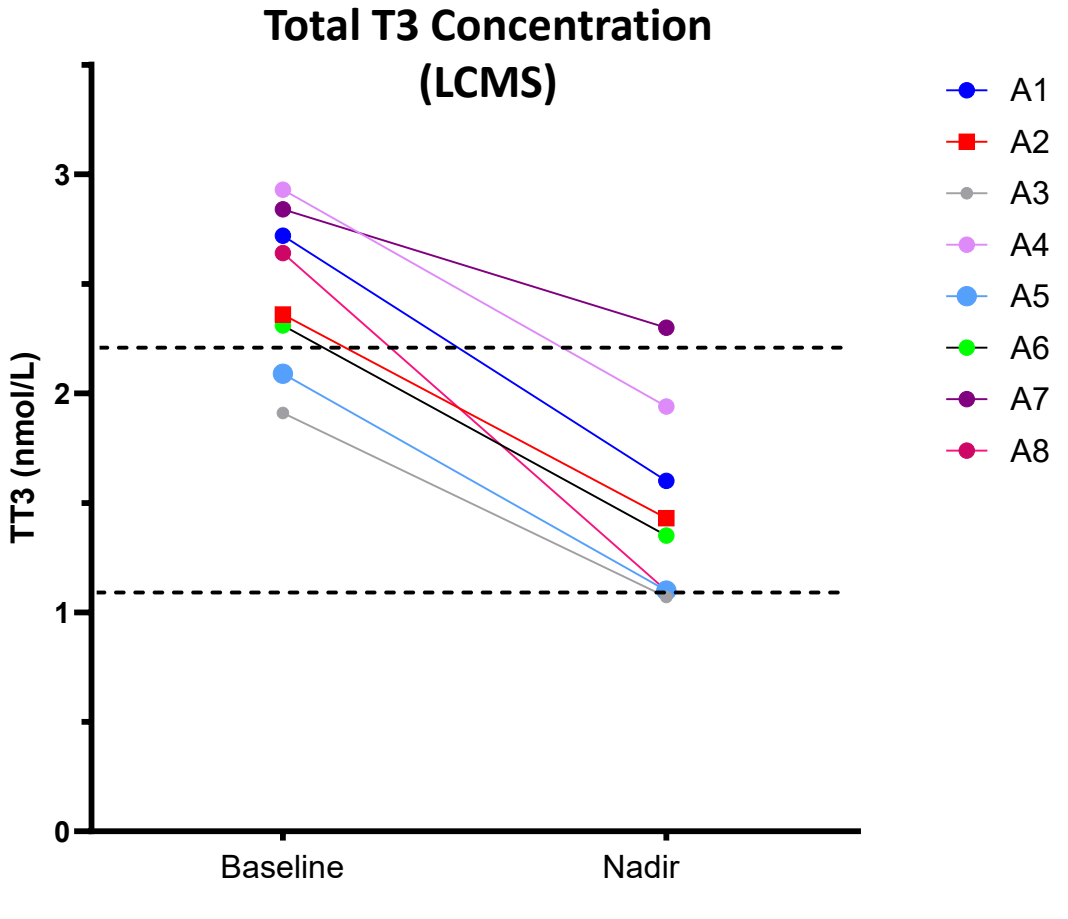


Welsh cohort
55 patients RTH Beta
2750 Age and sex matched controls
Median age 1st event 56 vs 67

Okosieme, Lancet Diabetes Endocrinology 2023. PMID 37475119

Thyroid Hormone Concentration on Triac Treatment





Appendix 7

Financials

Strong financial foundation for strategic execution

Solid cash position

- **Cash position August 21, 2025**: SEK 203 million
- **Number of outstanding shares:** 395,161,938
- **Market Cap:** ~SEK 2.6 billion* (~USD 274 million)
- **Listing venue:** Nasdaq Stockholm, Main Market; **Ticker:** EGTX

Largest shareholders

			↓ Capital
1	+	Frazier Life Sciences	16.73%
2	+	Peter Lindell	10.09%
3	+	Peder Walberg	7.33%
4	+	Fjärde AP-fonden	7.22%
5		Avla Holding AB	4.50%
6	+	The Invus Group	4.19%
7		Unionen	3.52%
8		Avanza Pension	2.84%
9		RegulaPharm AB	2.68%
10	+	Linc AB	2.10%
11	+	Woodline Partners LP	1.49%
12	+	Swedbank Robur Fonder	1.38%

Share issuance in Oct. 2025 for SEK 183m (USD 19m)

- Oversubscribed with participation from new & existing investors
- US biotech investors: Frazier Life Sciences, Invus, Petrichor & Woodline
- Swedish investors: Fjärde AP-fonden, Cidro Förvaltning (Peter Lindell), Linc & others

Note: * October 31, 2025

Egetis carried out directed share issuances amounting to SEK 300 million (USD 30 million)

Announcement published on September 30, 2024

- Led by Frazier Life Sciences with a USD 10 million investment.
- Supported by international and Swedish specialist healthcare funds.
- Subscription price at market price.

Egetis Therapeutics has successfully carried out directed share issuances amounting to SEK 300 million

September 30, 2024

NOT FOR PUBLICATION, DISTRIBUTION OR RELEASE, DIRECTLY OR INDIRECTLY, IN WHOLE OR IN PART, IN OR INTO THE UNITED STATES OF AMERICA, AUSTRALIA, CANADA, HONG KONG, ISRAEL, JAPAN, NEW ZEALAND, SOUTH AFRICA, SWITZERLAND OR ANY OTHER JURISDICTION WHERE SUCH PUBLICATION, DISTRIBUTION OR RELEASE WOULD BE UNLAWFUL OR REQUIRE REGISTRATION OR OTHER MEASURES.

Stockholm, Sweden, September 30, 2024. The Board of Directors of Egetis Therapeutics AB (publ) ("Egetis" or the "Company") (Nasdaq Stockholm: EGTX) has resolved on directed share issuances of in total 66,666,667 new ordinary shares at a subscription price of SEK 4.50 per share, corresponding to a 0.1 percent premium to the 5 day volume weighted average price (VWAP) preceding this announcement (the "Directed Issue"), through which the Company receives SEK 300 million (approximately USD 30 million) before transaction costs. The Directed Issue was oversubscribed and included both existing and new international and Swedish institutional investors. It was led by US healthcare investor Frazier Life Sciences with a USD 10 million investment, and supported by the international healthcare specialist Invus (USA/France), Platinum Asset Management (Australia), The Fourth Swedish National Pension Fund, Handelsbanken Fonder AB through the investment fund Hälsovård Tema (Sweden), Unionen (Sweden), HealthInvest Partners AB (Sweden) and Cidro Förvaltning AB (Sweden).

Egetis secured long-term financing of SEK 462m and added top-tier US specialist investor as largest shareholder

Announcement published on October 10, 2023

- **Unique combined long-term financing, comprising SEK 172m private placement at a premium and SEK 290m debt financing**
  - First in its class in a Swedish biotech setting, limiting dilution to existing shareholders and strengthening shareholder base

- **Private placement led by top-tier US healthcare specialist investor Frazier Life Sciences**
  - Demand for the new shares significantly exceeding the size of the private placement
  - Frazier Life Sciences new largest strategic shareholder in EGTX and brings significant sector expertise

- **SEK 290m debt financing obtained from BlackRock (formerly Kreos)**
  - Divided into two tranches, EUR 10m (“Tranche A”) and EUR 15m (“Tranche B”) which will become available provided that the Company reaches certain milestones, inter alia related to the phase III ReTRIACt study for Emcitate for Tranche B.
  - Egetis drew down Tranche A of the Debt Financing on November 30, 2023

FDA granted Rare Pediatric Disease designation to tiratricol

US Rare Pediatric Disease Priority Review Voucher (PRV) provides a ~$150m opportunity

Overview of PRV

- The FDA grants Rare Pediatric Disease designation (RPD) to therapies for serious or life-threatening diseases affecting fewer than 200,000 people in the USA
- Sponsors holding a RPD can apply to receive Priority Review Voucher (PRV) upon approval
- Provides accelerated FDA review of a new drug application for another drug candidate, in any indication, shortening time to market in the US
- The voucher may be sold or transferred to another sponsor
- During 2022-24 PRVs have been sold ranging from $100m-$158m

Examples of PRVs sold

Seller	Buyer	Value	Year
Marinus Pharmaceuticals	Novo Nordisk	$110M	2022
bluebird	argnx	$105M	2022
Biomarin	EliLilly	$110M	2022
Sarepta	Undisclosed	$102M	2023
Ipsen	Undisclosed	$158M	2024
PTC Therapeutics	Undisclosed	$150M	2024
Acadia	Undisclosed	$150M	2024
Zevra	Undisclosed	$150M	2025

Under the terms of the acquisition of RTT in Q3 2020, 50% of the potential net proceeds from a sale of a PRV related to Emcitate should be paid as an earnout to the sellers of RTT

Egetis submits patent application to the USPTO

- Patent application for “Processes of Preparation” of tiratricol
- Processes and compounds described in the patent application
- If granted, this would be a significant patent for Egetis
- Generally, the exclusivity term of a new patent is 20 years from the date on which the application for the patent was filed in the United States.

Egetis submits a patent application to the United States Patent and Trademark Office for “Processes of Preparation” of tiratricol

Stockholm, Sweden, September 19, 2024. Egetis Therapeutics AB (publ) (“**Egetis**” or the “**Company**”) (Nasdaq Stockholm: EGTX), today announced that it has submitted a patent application with the United States Patent and Trademark Office (USPTO) for “Processes of Preparation” of tiratricol. If granted, this would be a significant patent Egetis has obtained for the investigational drug tiratricol.

Tiratricol is an endogenously available metabolite of thyroid hormone, with similar bioactive properties as the active thyroid hormone T3. Tiratricol enters the cell independently of the monocarboxylate transporter 8 (MCT8), bypassing the pathophysiologic defect in MCT8 deficiency. Clinical trials for the use of tiratricol for the treatment of MCT8 deficiency are ongoing and in October 2023 Egetis submitted a marketing authorisation application (MAA) in the EU. Accordingly, new and more efficient synthetic routes leading to tiratricol are needed. The processes and compounds described in the patent application help meet these and other needs.

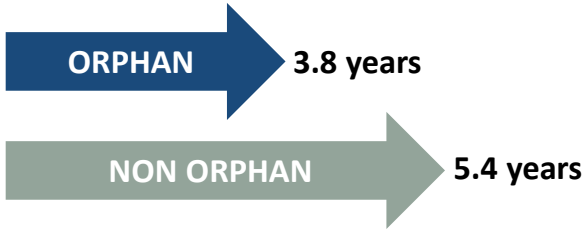
Appendix 8

The attractiveness of the orphan drug segment

Orphan drug segment – a highly attractive opportunity

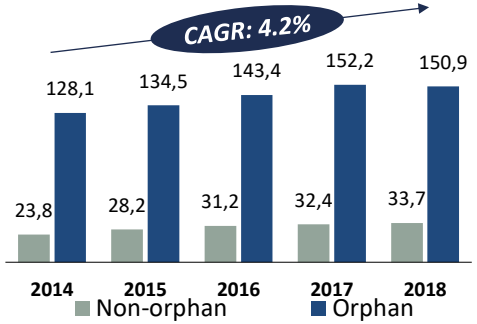
Shorter clinical development time[1]

Phase II to launch Average # of years



Higher attainable prices[2]

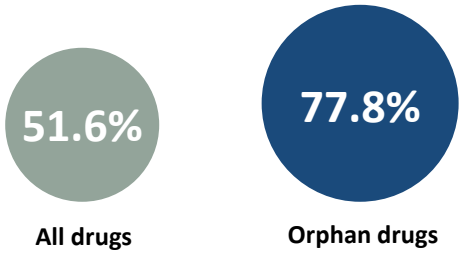
Mean cost per patient and year (USDk)



Higher probability of success[3]

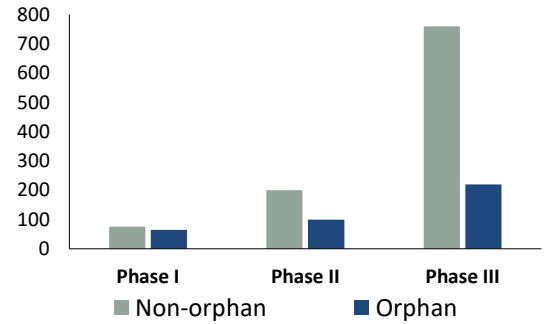
Phase III to approval

POS in metabolic/endocrinology indications

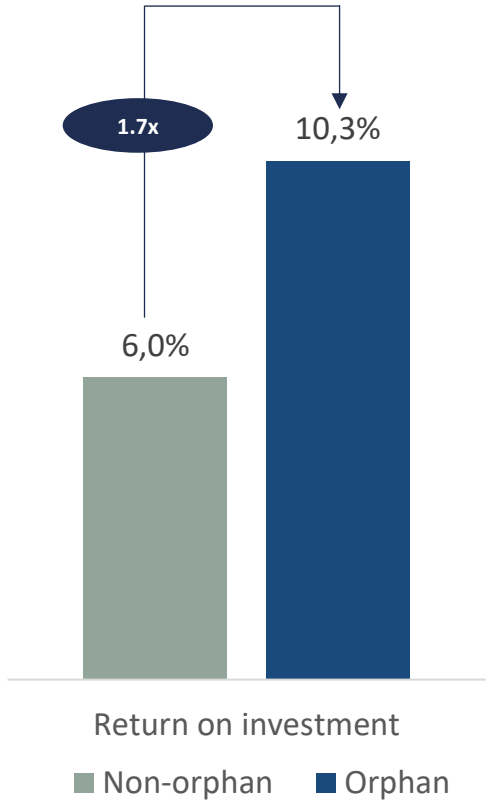


Fewer patients for clinical trials[4]

Patients per trial



Orphan drugs attractive returns[5]



Source: (1) Orphan drug development: an economically viable strategy for biopharma R&D, Meekings, Williams & Arrowsmith, 2012; (2) EvaluatePharma; (3) Estimation of clinical trial success rates and related parameters, C. Wong, K. Siah, A. Lo, Biostatistics, 2019; (4) BioMed Central; (5) EvaluatePharma Orphan Drug Report 2013

Note: Orphan Drugs: Populations of less than 5/10,000 inhabitants in the EU or <200,000 inhabitants in the US

Orphan drug segment – a highly attractive opportunity

1. **Orphan drug designation is awarded to products targeting limited disease populations[1]**
2. **More than 7,000 known rare diseases**
3. **Approx. 10% of the general population may be affected by a rare disease**
4. **Substantial unmet medical need for patients, only 5% of rare diseases have an approved therapy**

Development

- Less extensive clinical trials
- Agile and faster development process
- Lower costs
- Lower development risk

Registration

- Free regulatory advice
- Reduced fees
- Expedited review
- Market exclusivity

Market

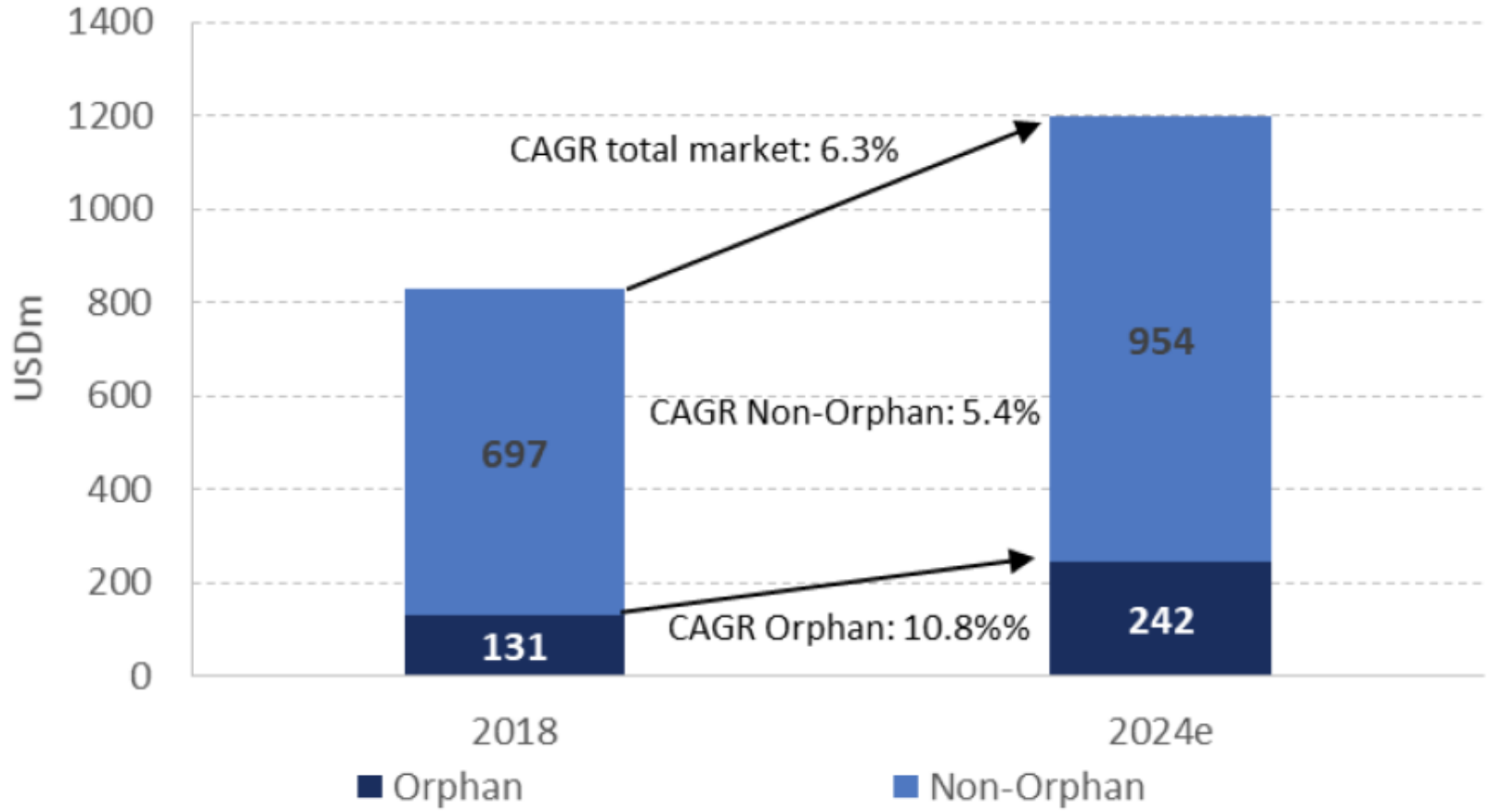
- No or few competitors
- Highly focused target groups
- Premium pricing

Well-defined patient populations with substantial unmet medical need

Note: (1) Populations of less than 5/10,000 inhabitants in the EU or <200,000 inhabitants in the US

CAGR estimates of total pharmaceutical market vs orphan

The global orphan or rare disease market size was valued at an estimated USD 140 – 150 bn and is expected to grow at 10-14% CAGR over the coming five years.



Source: EvaluatePharma, Pareto.

Appendix 10

Leadership Team and Board of Directors

Leadership team with global experience & proven track record

Nicklas Westerholm
CEO
- Joined 2017
- AstraZeneca 1995-2017
- VP Late-stage development CVMD
- Executive Officer & VP Japan Operations
- Director Investor Relations

Desiree Luthman
VP Regulatory Affairs
- Joined 2023
- Global regulatory professional, >25y experience
- Passage Bio, Verona Pharma, Sanofi, BMS, Celgene, AstraZeneca

Katayoun Welin-Berger, PhD
VP Technical Operations
- Joined 2023
- VP Operations at Calliditas Therapeutics
- Previously at BioGaia and AstraZeneca

Yilmaz Mahshid, PhD
CFO
- Joined 2021
- Investment Manager & Controller at Industrifonden
- Sell-side analyst at Pareto & Öhman
- CEO Medivir

Kristina Sjöblom Nygren, MD
CMO
- Joined 2020
- CMO, Head of Development at Santhera
- 18 years at SOBI, Wyeth & AstraZeneca
- Worked as physician in clinical positions

Anny Bedard
President Egetis North America
- Joined 2022
- Commercial leadership roles at Shire and Sarepta

Christian Sonesson, PhD
VP Product Strategy & Development
- Joined 2017
- AstraZeneca 13 years
- Late-stage development expertise from FORXIGA, MOVANTIK, ONGLYZA, BRILINTA & QTERN

Henrik Krook, PhD
VP Commercial Operations
- Joined 2020
- Commercial roles at Alexion, Novartis, Roche and Affibody

Nils Hallen
Global Head of HR
- Joined 2021
- Adjunct professor in work & organizational psychology

Laetitia Szaller
General Counsel & Head of Compliance
- Joined 2023
- Senior legal roles at AM Pharma, UCB & Zoetis

Karl Hård, PhD
VP IR & Business Development
- Joined 2022
- Redx Pharma, Optimum Strategic Communications, Kiadis, AstraZeneca

Board of directors

Mats Blom

Chair of the board since 2024

- Shares in Egetis: 3,134,762
- BA, Business Administration & Economics, Lund University; MBA, IESE University of Navarra
- Other assignments: CFO NorthSea Therapeutics, Board member Hansa Biopharma, Auris Medical, Altamira Therapeutics & Pephexia Therapeutics

Gunilla Osswald

Board member since 2017

- Shares in Egetis: 40,000
- PhD in biopharmacy and pharmacokinetics
- Other assignments: CEO BioArctic AB

Behshad Sheldon

Board member since 2023

- Shares in Egetis: 0
- BS in neuroscience
- Other assignments: Chair of the Board of FORCE (Female Opioid Research and Clinical Experts) in Princeton, NJ, Board Member, Camurus AB and Maxona Pharmaceuticals; EVP & MD, Biotech Value Advisors

Margarida Duarte

Board member since 2025

- Shares in Egetis: 0
- BS in Pharmaceutical Sciences & Executive Master's degree in Medical Marketing Management
- Other assignments: Executive Vice President, Global Chief Commercial Officer, Deciphera Pharmaceuticals

Elisabeth Svanberg

Board member since 2017

- Shares in Egetis: 37,676
- MD, PhD, Assoc Professor in surgery
- Other assignments: Chief Development Officer Ixaltis SA. Board member Leo Pharma, Amolyt Pharma, Galapagos and EPICS Therapeutics

Termination of discussions regarding a potential acquisition of the Company

Announcement published on May 23, 2023

- Discussions, triggered by an unsolicited approach by an external party, have taken place between certain external parties and Egetis regarding a potential acquisition of the Company
- Discussions have now been terminated as the Board believes the contemplated offer and terms, while providing a premium to the current share price, considerably undervalued the long-term prospects of the Company
- *"A transformative period for the Company, with several near-term value creating milestones and the Board of Egetis believes that the strategy to build an independent sustainable rare-disease company life remains the most long-term value creating alternative for our shareholders"*
- As a consequence of this intense process and discussions, the timeline for the submission of the marketing authorisation application (MAA) for *Emcitate* (tiratricol) to the European Medicines Agency (EMA) has been extended from the second quarter to the early autumn of 2023*

* *Emcitate* MAA filed in October 2023. Positive CHMP opinion received in December 2024. EU approval Feb 2025.

Appendix 11

Paracetamol/Acetaminophen overdose and clinical experience with Aladote

* In-house development of *Aladote* has been parked until *Emcitate* MCT8 deficiency submissions have been completed

Aladote® – To prevent acute liver injury caused by paracetamol poisoning*

- Paracetamol poisoning is one of the most common overdoses with >175,000 hospital admissions globally per annum
- No adequate treatment exists for increased risk patients
- Orphan drug designation (ODD) granted in the US & EU
- Successful results from Phase Ib/IIa study in paracetamol overdosed patients
- Pivotal Phase IIb/III study planned for marketing authorization application in both US and EU
- No competing products in clinical development
- In-house development parked until *Emcitate* submissions have been completed for MCT8 deficiency

*In-house development of *Aladote* parked until *Emcitate* submissions have been completed

Paracetamol/acetaminophen poisoning

– no adequate treatment for increased-risk patients

What is paracetamol/ acetaminophen poisoning?

- Minimum toxic dose of paracetamol/acetaminophen in adults is only **7.5g**
- Risk factors include malnutrition, alcoholism and consumption of other medications
- Paracetamol/acetaminophen poisoning can lead to **acute liver failure, liver transplant** or **death**

How many does it affect?

- **19 billion** units of paracetamol /acetaminophen packages are sold in the US alone every year
- **>175,000 patients hospitalised globally per annum** driven by 89,000 cases/year of paracetamol overdose in the US and 105,000 cases/year in the UK (~ 50% hospitalised)
- ~50% of paracetamol overdose cases are unintentional

Why is current treatment inadequate?

- Efficacy of current NAC (N-acetylcysteine) treatment decreases with time
- Approximately **25% of patients are late arrivals** to hospitals (>8h) – late arrivals are **at increased risk**
- There is **no effective treatment option for patients at increased risk**

A new standard of care is needed

- **Aladote®** aims to become **a new standard of care** for patients with increased risk for liver injury in combination with NAC

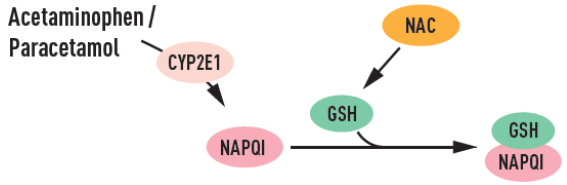
© 2024 Egetis Therapeutics. All rights reserved.

Orphan drug candidate

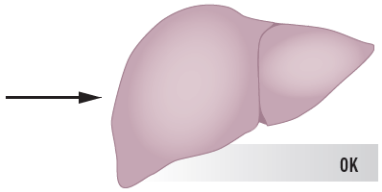
with clear scientific and mechanistic rationale

Early presenters (<8h)
NAC treatment effective against liver injury

- Liver glutathione (GSH) replenished by NAC, toxic NAPQI metabolite excreted as GSH conjugate

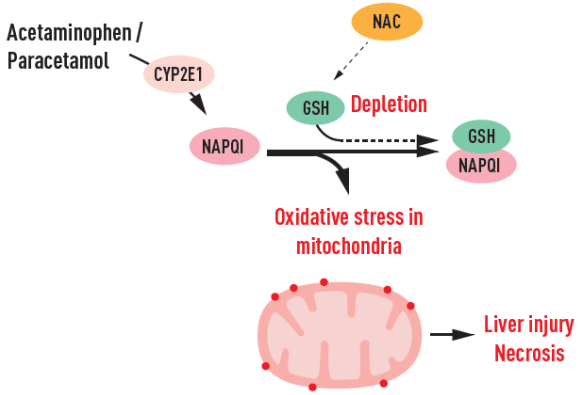


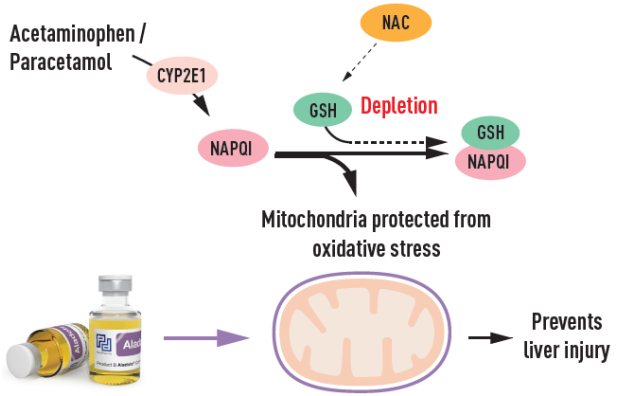
- In most cases NAC effectively prevents liver injury i.e. limited need for Aladote®



Late presenters (>8h) are at increased-risk for liver injury
NAC treatment + Aladote® to prevent liver injury

- **Under NAC treatment alone** liver GSH stores depleted by the toxic NAPQI metabolite -> **oxidative stress, mitochondrial dysfunction and liver injury (necrosis)**





- **Aladote®** (calmangafodipir) prevents ROS and RNS formation, restores mitochondrial energy production and **prevents liver injury**

Source: Akakpo et al. 2020, Burke et al. 2010.

Reactive nitrogen species (RNS), Reactive Oxygen Species (ROS)

© 2024 Egetis Therapeutics. All rights reserved.

Overview of completed Phase Ib/IIa

Primary objective and results	• Met primary endpoint of safety tolerability in the combination of Aladote® and NAC • Results presented at the 58th Annual Meeting of the Society of Toxicology, EASL ILC in April, Vienna and published in Lancet's journal EBioMedicine in 2019 • Presented at, American College of Medical Toxicology (ACMT) and Society of Toxicology (SOT), as novel emerging treatments for acetaminophen/ paracetamol toxicity in 2021
Secondary objectives and results	• Measurements of Alanine transaminase (ALT), international normalised ratio (INR), keratin-18, caspase-cleaved keratin-18 (ccK18) and microRNA-122 (mir122) and glutamate dehydrogenase (GLDH) indicates that Aladote® reduce liver injury
Description	• An open label, rising-dose, randomized study exploring safety and tolerability of Aladote® co-treatment with NAC • ClinicalTrials.gov identifier: NCT03177395
# of patients	• Single ascending dose study in 3 dosing cohorts of 8 patients (N=24) as add-on to NAC regime
Timetable	• Initiated in June 2017 (first patient in) • Completed in September 2018


EBioMedicine 46 (2019) 423–430

Contents lists available at ScienceDirect

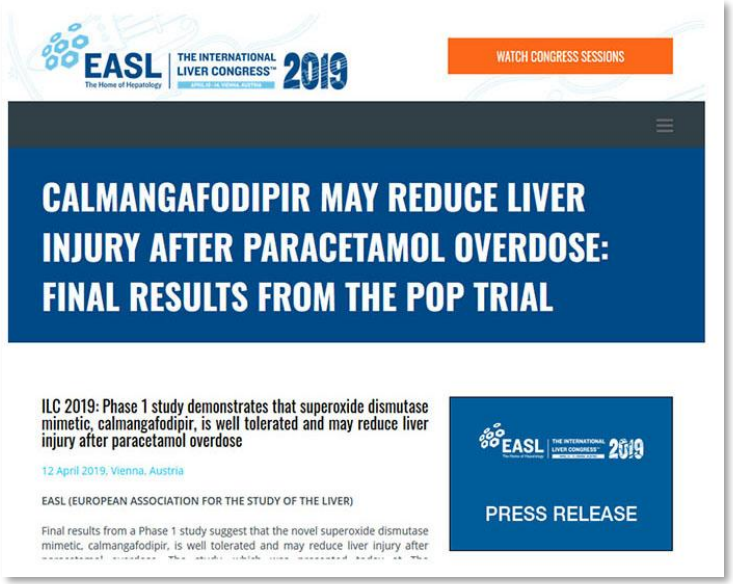
EBioMedicine

journal homepage: www.ebiomedicine.com

EBioMedicine
Published by THE LANCET

Principal results of a randomised open label exploratory, safety and tolerability study with calmangafodipir in patients treated with a 12 h regimen of N-acetylcysteine for paracetamol overdose (POP trial)

Emma E. Morrison [a], Katherine Oatey [b], Bernadette Gallagher [c], Julia Grahamslaw [c], Rachel O'Brien [c], Polly Black [c], Wilna Oosthuyzen [a], Robert J. Lee [b], Christopher J. Weir [b], Dennis Henriksen [d], James W. Dear [a,*], On behalf of the POP Trial Investigators [1]



© 2024 Egetis Therapeutics. All rights reserved.

Positive proof-of-principle Phase Ib/IIa results

Indicates that Aladote may reduce liver injury

Safety & tolerability

Event	NAC alone	NAC + 2 µmol/kg Aladote	NAC + 5 µmol/kg Aladote	NAC + 10 µmol/kg Aladote
Any AE	6 (100%)	6 (100%)	6 (100%)	6 (100%)
Any SAE	2 (33%)	4 (67%)	2 (33%)	3 (50%)
SAE Starting within 7 days	1 (17%)	1 (17%)	1 (17%)	2 (33%)

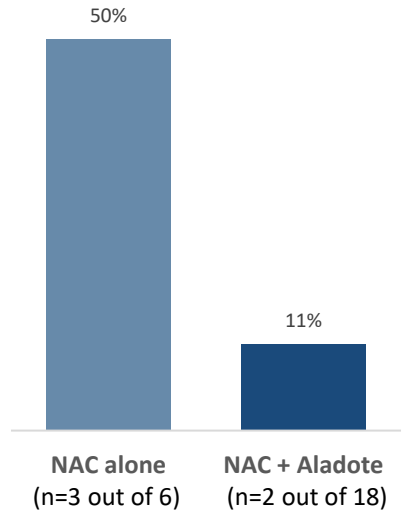
- Met primary endpoint of safety tolerability in the combination of Aladote® and NAC
- No AE or SAE probably or definitely related to Aladote®

Liver injury – ALT[1] pre-defined secondary outcome

Event	NAC alone	NAC + 2 µmol/kg Aladote	NAC + 5 µmol/kg Aladote	NAC + 10 µmol/kg Aladote
50% ALT increase	2 (33%)	0 (0%)	0 (0%)	1 (17%)
100% ALT increase	1 (17%)	0 (0%)	0 (0%)	1 (17%)
ALT >100 U/L at 10 hours	2 (33%)	0 (0%)	0 (0%)	0 (0%)
ALT >100 U/L at 20 hours	2 (33%)	0 (0%)	0 (0%)	0 (0%)

- ALT >100 U/L is the indication to stay in hospital

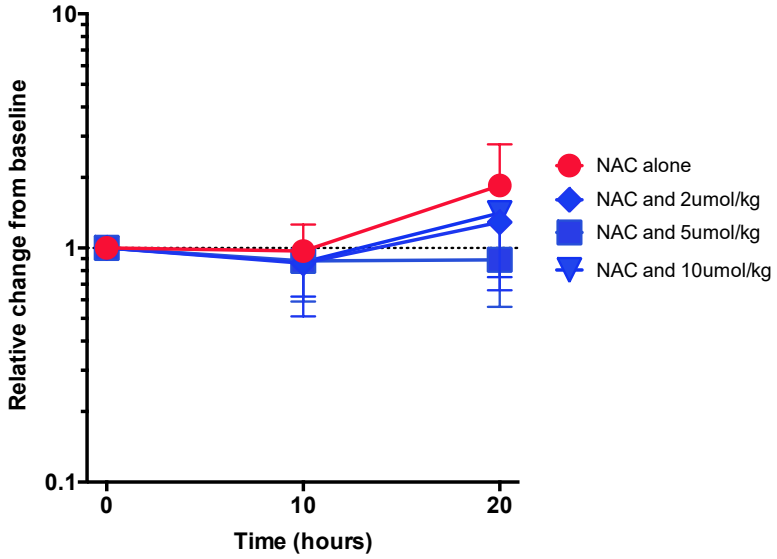
% of patients needing additional NAC infusions after planned 12h NAC infusion



Note: (1) Alanine transaminase (ALT) is a transaminase enzyme found in plasma and in various body tissues especially the liver's hepatocytes. Serum ALT is commonly measured clinically as part of a diagnostic evaluation of hepatocellular injury, to determine liver health

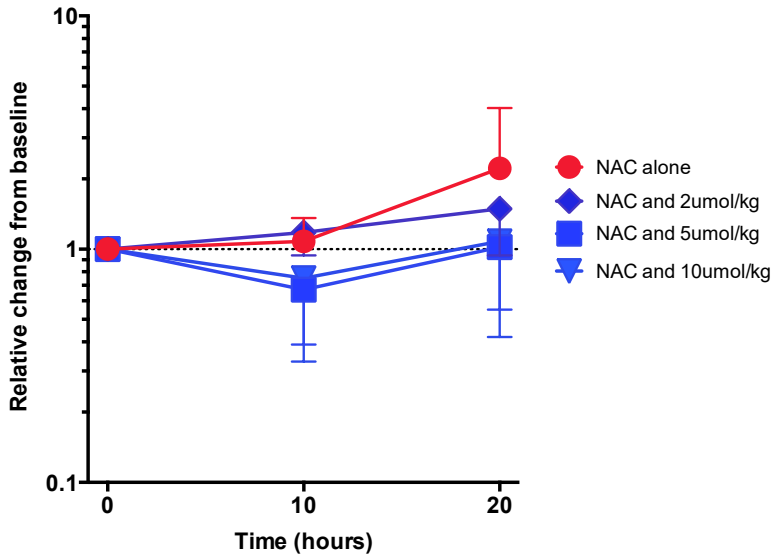
Aladote® demonstrates consistent results of reduced liver injury as measured by exploratory biomarkers

K18



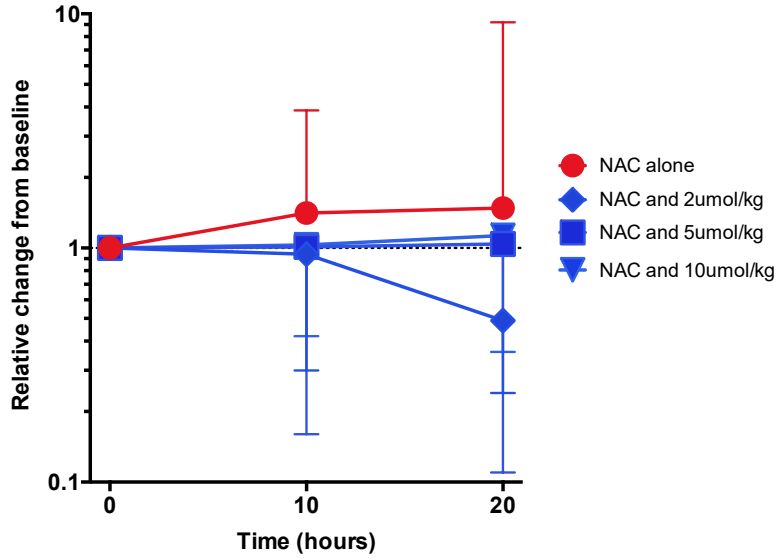
K18 is a measure of cell death and correlate with peak ALT activity during the hospital stay

ccK18



ccK18, is a measure of cell death and correlate with peak ALT activity during the hospital stay

miR-122



miR-122 is a liver specific early marker (micro-RNA) for acute liver injury which predicts a rise in ALT activity following paracetamol overdose

3.

*Aladote® - Regulatory pathway to submissions in EU and US**

* In-house development of *Aladote* has been parked until *Emcitate* MCT8 deficiency submissions have been completed

ALBATROSS: Phase IIb/III study for US/EU regulatory submission*

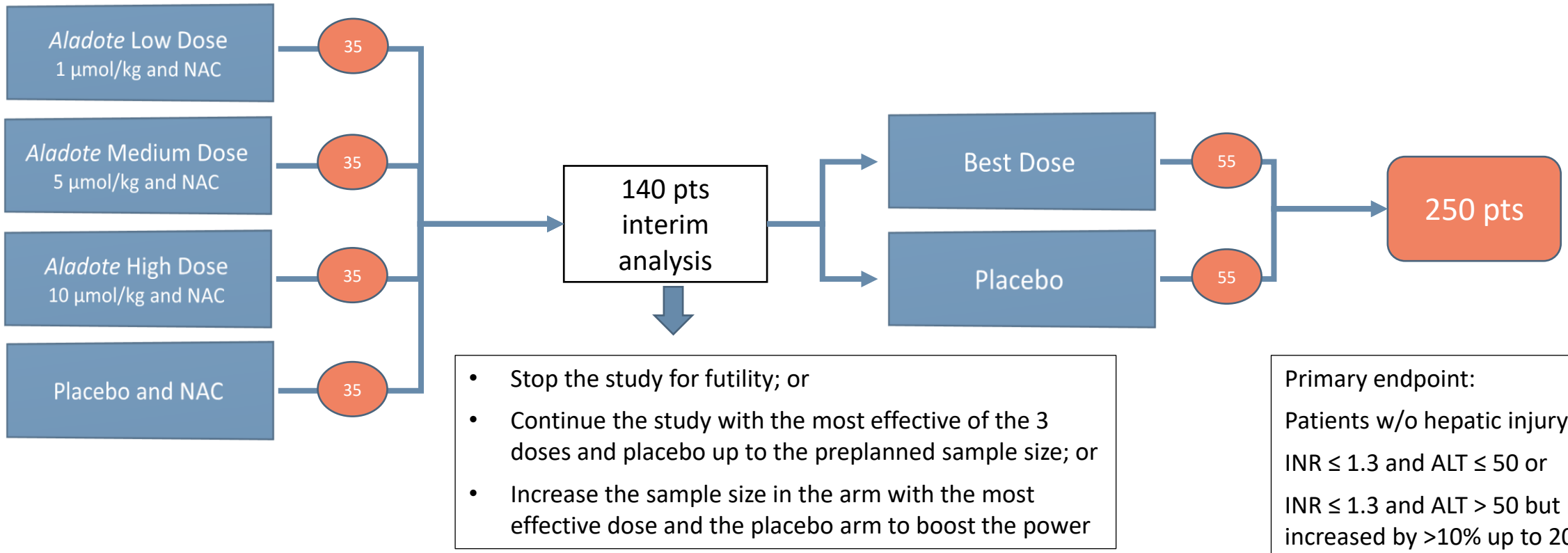
Patient population	• Patients who have overdosed on paracetamol with increased risk of liver damage due to late arrival at hospital (> 8h) who need treatment with NAC
NAC regimen	• Approved 21 hours NAC regimen
Treatment groups	• 4 groups in combination with NAC: *Aladote* high dose; *Aladote* middle dose; *Aladote* low dose; Placebo
Initiation of active treatment	• IV (bolus) as soon as possible after randomization and after starting NAC treatment (but no later than 4 hours after starting NAC treatment)
Interim analysis	• Interim analysis after 35 patients per treatment group, which includes a futility analysis, dose selection and analysis of continued study size (number of patients)
Study size	• 250 patients planned
Efficacy endpoints	• Primary: Combination of ALT and INR • Number (%) of patients who need extended NAC treatment after 21 hours • Length of hospital stay • Explorative biomarkers: K18, miR-122 and GLDH
Study countries	• EU, UK and USA

*Study parked until *Emcitate* submissions have been completed

ALBATROSS: *Aladote* Phase IIb/III study design

Seamless Phase IIb/III design

Based on the acetaminophen/paracetamol levels eligible patients will be randomised in a 1:1:1:1 ratio to one of the 4 treatment arms in combination with NAC:



- Stop the study for futility; or
- Continue the study with the most effective of the 3 doses and placebo up to the preplanned sample size; or
- Increase the sample size in the arm with the most effective dose and the placebo arm to boost the power

Primary endpoint:

Patients w/o hepatic injury

INR ≤ 1.3 and ALT ≤ 50 or

INR ≤ 1.3 and ALT > 50 but not increased by >10% up to 20h

Aladote clinical development timelines

2022

- ✔ Orphan Drug Designation EU
- ✔ CTA pivotal Phase IIb/III study

tbc

- Start pivotal Phase IIb/III study (after *Emcitate* submissions have been completed)

tbc

- Interim analysis
- Recruitment completed and topline results

tbc

- Regulatory submissions Europe/US
- Europe/US approvals and launch
- Regulatory submissions ROW

Orphan drug designation in US and EU
Composition of matter patent expires in 2032
Method of use patent until 2037

3.

Aladote® - Commercial opportunity

Aladote– alleviating patient and societal burden

Aiming to provide value for both patients and society

POD is a life threatening condition with remaining medical needs

Patients

- POD (paracetamol/acetaminophen overdose) can lead to acute liver failure, liver transplant or death
- In US and UK together, yearly > 500 deaths due to POD and more people registered for liver transplantation

Society

- In the US the annual cost has been estimated at > $1bn to treat patients with POD[1]
- The POD Emergency Department and inpatient cost is approximately USD 13-40k[1]
- The average POD inpatient length of stay is 3.1 days with a variance of +4.4 days for the most severe cases[1]
- US liver transplant costs USD 125-473k[1]

With **Aladote**, the ambition is to **reduce hepatic injury** of POD and thereby contribute to **fewer hospitalization days**, **prevent need** for liver transplantation and **increase survival**

Source:; (1) Adapted from: Altyar A. Clinical and economic characteristics of emergency department visits due to acetaminophen toxicity in the USA BMJ Open 2015;5;

Commercialisation of *Aladote* for high-risk POD patients

Very cost-effective since possible to launch through members of Emcitate team

Favorable conditions for launch success

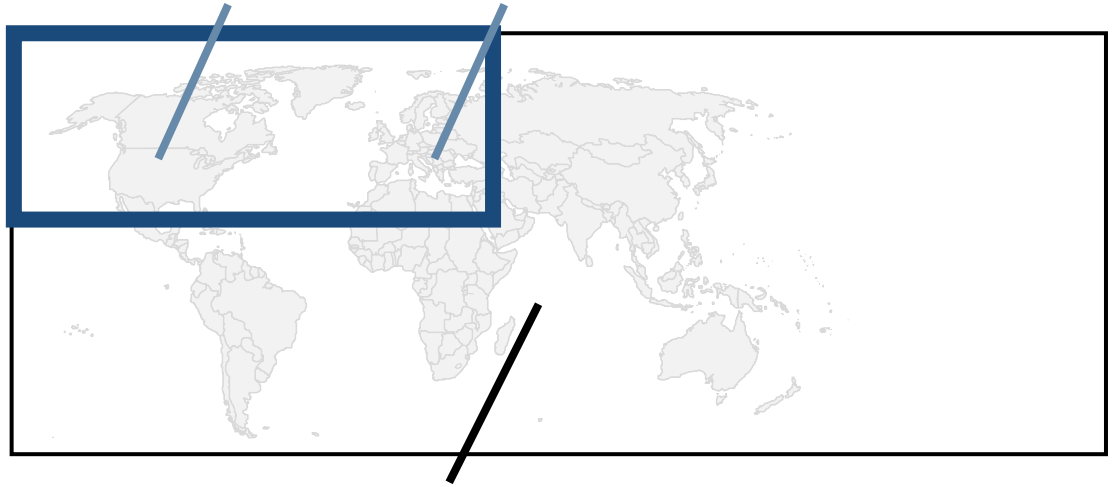
Addressing unmet medical need	☑
Leading KOL support	☑
Centralized**, focused target groups** of **specialists** eager to improve care	☑
Treatment choice **highly protocol driven**	☑
No competition	☑

Addressing life-threatening condition

- Anologue antidotes priced at $3.5k – 50k
- National emergency hospital stocking guidelines gives opportunity to work through **small team** and still ensure **rapid sales uptake**

Hospitalized POD patients per year

US: > 40,000* patients Europe: > 140,000* patients



Commercialization in rest of world managed through partners

*Annual number of POD (paracetamol/acetaminophen overdose) cases hospitalized and receiving i.v. antidote (NAC currently the only option), 25% late arrivals (>8h)

Analogue antidotes priced at $ 3.5k – 50k

National emergency hospital stocking guidelines - opportunity for rapid market penetration

- Various antidotes, e.g. vs. drug overdosing, metal poisoning, snake bites and reversal of anticoagulant treatment effects
- Limit morbidity/mortality when used within appropriate time
- National recommendations for stocking of antidotes at hospitals providing emergency care
  - For getting payer/formulary committee acceptance to be stocked, antidotes are in general priced lower than traditional orphan drugs, despite often having orphan status
  - Getting included provides great opportunity for rapid market penetration
    - Praxbind stocked in 3,200 US hospitals < 3 years from launch
    - Andexxa sales $112mn in US alone second year on market
- Analogue antidotes for comparable settings as Aladote have global average costs of $ 3.5k – 50k per treatment

	Naloxone hydrocloride	Praxbind	Andexxa/Ondexxya	Aladote (target profile)
Year of first approval	1971	2015	2018	NA
Poisoning indication	Opioid toxicity	Reversal of anticoagulant effects of the NOAC dabigatran	Reversal of anticoagulant effects of the factor Xa inhibitors apixaban & rivaroxaban	Paracetamol/ acetaminophen toxicity
Cost per treatment	Low since generic	$ 3.5k – 4.5k	$ 25k – 50k	TBD

EGETIS THERAPEUTICS

Thank you!

Egetis Therapeutics
egetis.com
karl.hard@egetis.com