



## Corporate presentation

June 2023

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

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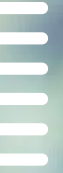
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# Agenda



1. An integrated orphan drug company, focusing on late-stage development for commercialization
2. Emcitate®
  - Overview of MCT8-deficiency
  - Clinical experience with Emcitate
  - Regulatory pathway to submissions in EU and US
  - Commercial opportunity
3. Aladote®
  - Paracetamol/Acetaminophen overdose and clinical experience with Aladote
  - Regulatory pathway to submissions in EU and US
  - Commercial opportunity
4. The orphan drug segment
5. Summary
- A. Appendix

WE CARE  
FOR THE RARE



1.

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

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



Listed on NASDAQ Stockholm (EGTX)

HQ in Stockholm, Sweden

~30 FTEs

1

Dedicated orphan drug company  
Two late-stage assets: ***Emcitate*** and ***Aladote***

2

Target **MAA/NDA** submissions:  
***Emcitate 2023*** and ***Aladote 2025***

3

Highly attractive **orphan drug segment** with potential  
**>\$1Bn annual sales opportunity**

4

Plan to **launch** through **small in-house commercial**  
organization in the EU and North America

5

**Strong team** with late-stage orphan clinical development,  
registration and commercialization experience from:



# Building a sustainable orphan drug company

WE CARE  
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- Successfully develop *Emcitate* and *Aladote* for market approvals in 2024 and 2025/26, respectively
- Commercialize *Emcitate* and *Aladote* through an inhouse focused 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 extend and improve quality of life

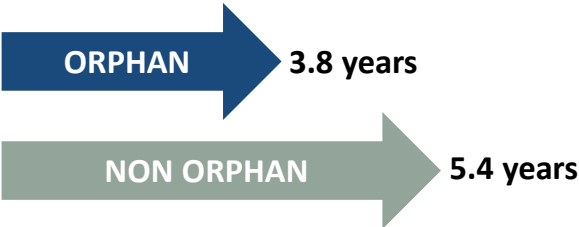
To create value for patients, society and shareholders by developing and providing a portfolio of unique products for the treatment of rare diseases with substantial medical need



# Orphan drug segment – a highly attractive opportunity

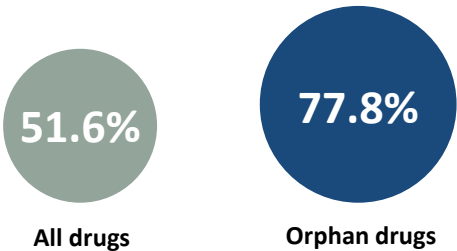
## Shorter clinical development time<sup>1</sup>

Phase II to launch Average # of years



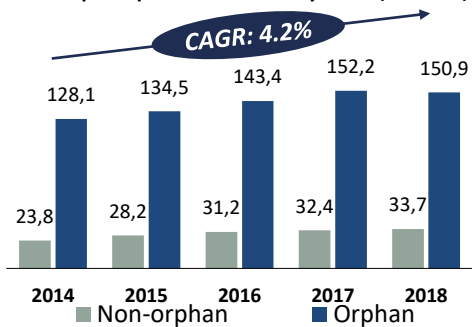
## Higher probability of success<sup>3</sup>

Phase III to approval  
POS in metabolic/endocrinology indications



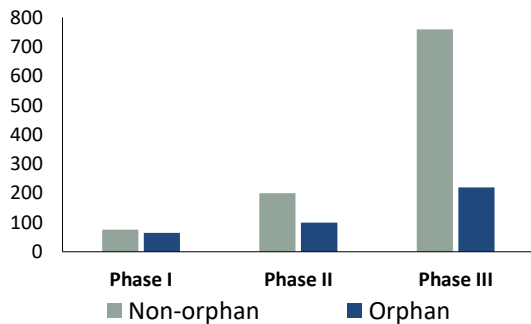
## Higher attainable prices<sup>2</sup>

Mean cost per patient and year (USDk)

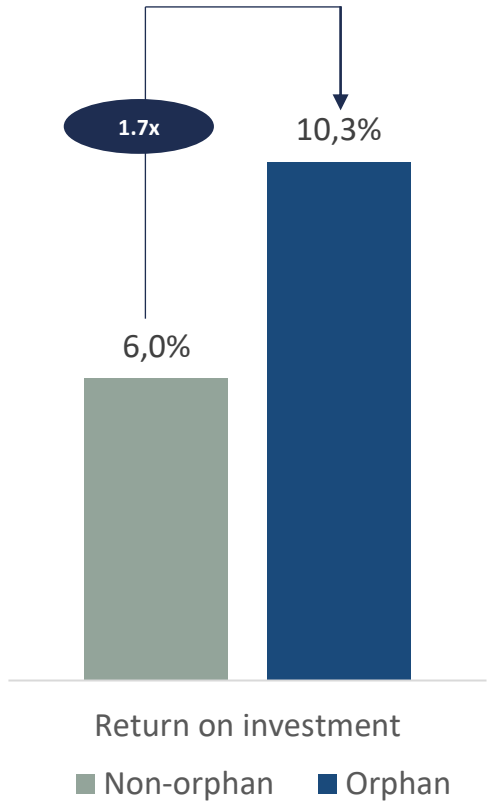


## Fewer patients for clinical trials<sup>4</sup>

Patients per trial

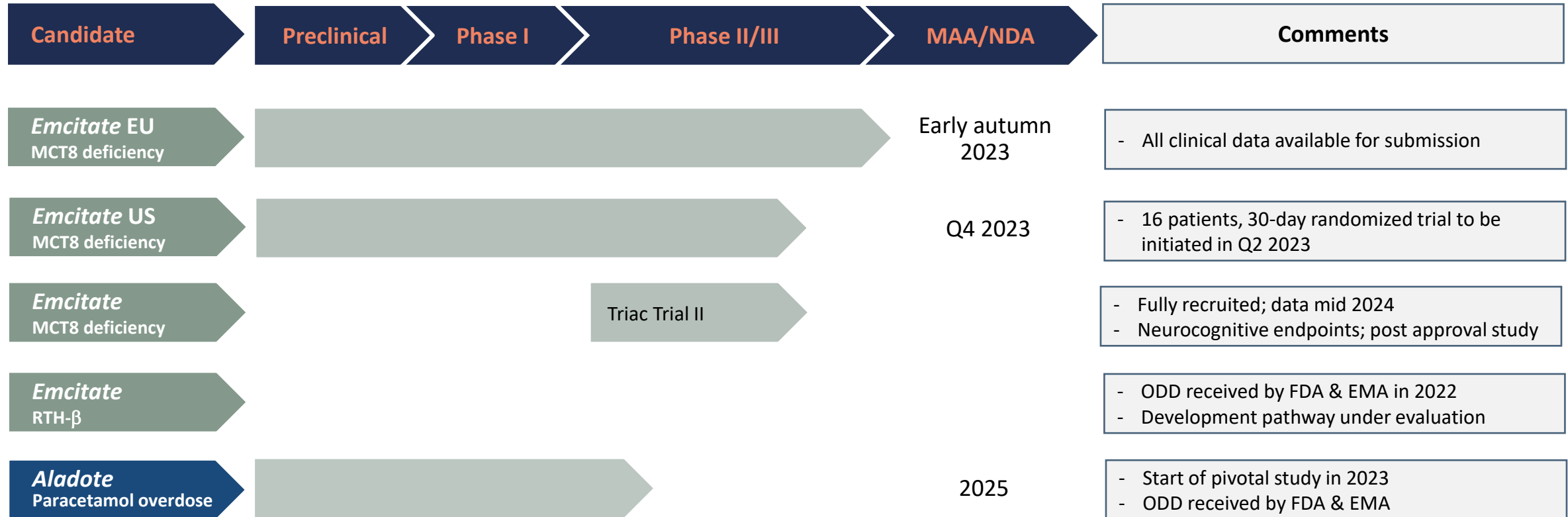


## Orphan drugs attractive returns<sup>5</sup>



# Pipeline overview

*Planned Emcitate EU and US filings in 2023*



# Two highly promising orphan drug candidates

## Emcitate® – Therapy for MCT8 deficiency

- MCT8 deficiency affects ~1:70,000 males: high unmet medical need, no available treatment. No competing sponsored products in clinical development
- Orphan Drug Designation in EU & US
- US Rare Pediatric Disease Designation, eligible for **Priority Review Voucher**. Fast track designation granted by FDA
- Triac Trial I (Phase IIb) completed with **significant** and **clinically** relevant effects on **T3 levels** and **chronic thyrotoxicosis**
- Real-world data published **2021 confirms long-term efficacy and safety** of *Emcitate*
- **MAA** in **early autumn 2023** based on existing clinical data
- **NDA** in **Q4 2023**, after conducting a 30 days placebo-controlled study (ReTRIACt) in 16 patients to verify the results on T3
- **Triac Trial II fully recruited**; to establish the effects of early intervention on **neurocognitive** development, previously seen in Triac Trial I. Results expected mid 2024
- Around **180 patients** are being **treated** with *Emcitate* on a **named patient basis** – Expanded Access Program implemented as requested by the FDA

## 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, targeting study start in 2023
- No competing products in clinical development

# Commercialisation of *Emcitate* & *Aladote*

*Commercial infrastructure build up initiated*



## Strong success factors...

- 1 High unmet medical need without competing compounds
- 2 Centralized, **focused target** groups of **specialists**
- 3 **Top-down** scientific **sales approach**
- 4 Leading KOL support
- 5 Treatment algorithms **highly protocol driven**



## ...for sustainable, profitable & lean commercialisation

- Building **inhouse commercial capabilities** for launch of *Emcitate*® and *Aladote*® in EU and US
- **Small and focused footprint** with an estimated < 50 FTEs considered sufficient for both assets
- Retain **larger share of product revenues** over time within Company
- **Commercialisation** in other territories through **partners**

## 2.

### *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 2002 the first thyroid hormone transporter (MCT8) was identified
  - 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

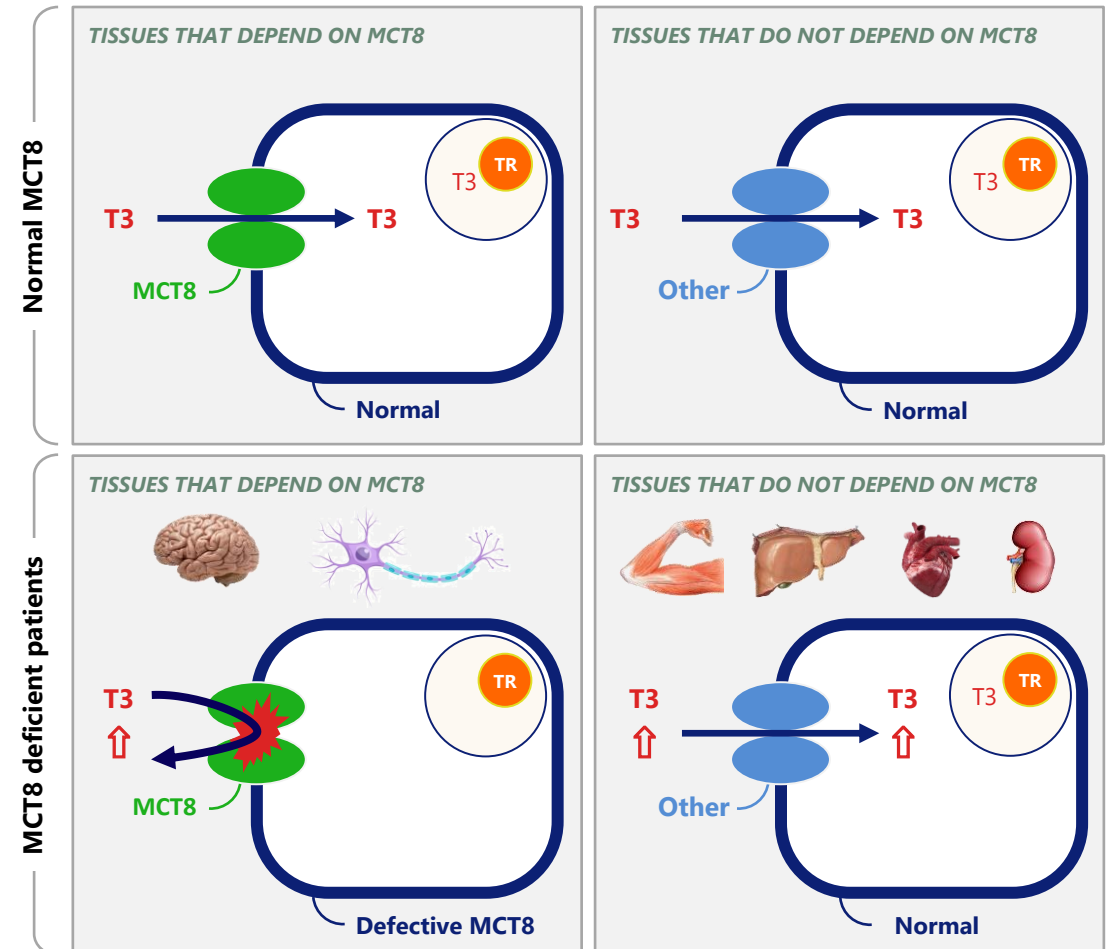
## MCT8 Plays a Key Role in Neurocognitive Development

- MCT8 is the only thyroid hormone transporter in the cells of the blood brain barrier and neurons
  - The human brain is dependant 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



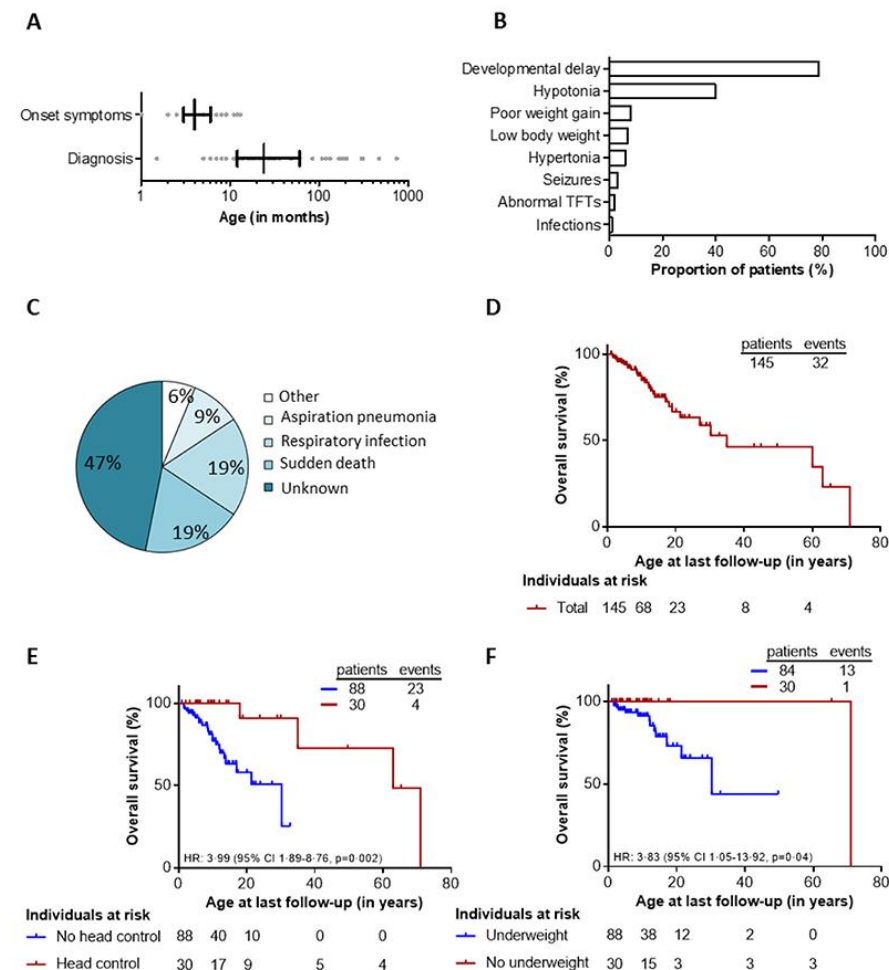
What is MCT8 deficiency?	What does it mean?	What are the challenges?	How do you manage the disease?	Quick facts from natural history <sup>2</sup>																				
<ul style="list-style-type: none"><li>Genetic X-linked disorder</li><li>Impaired thyroid hormone trafficking across cellular membranes</li><li>MCT8 is a key thyroid hormone transporter in the body</li><li>Prevalence 1:70,000 males</li></ul> <div></div> <p>Patients with MCT8 Deficiency<sup>1)</sup></p>	<ul style="list-style-type: none"><li>Non-functional MCT8 protein: T3 cannot cross blood-brain-barrier</li><li>Low amounts of thyroid hormone in the brain &amp; CNS</li><li>Disrupted feedback loop results in a compensatory increase in circulating thyroid hormone</li></ul> <div></div> <ul style="list-style-type: none"><li>Simultaneous too high &amp; too low thyroid hormone in different tissues</li></ul>	<ul style="list-style-type: none"><li>Patients appear normal at birth</li><li>Initial symptoms within the first months of life</li><li>Severe intellectual disability</li><li>Most patients never able to sit or walk; limited ability to communicate</li><li>Life-long morbidity: agitation, CV symptoms, wasting &amp; impaired life expectancy</li></ul> <div></div> <ul style="list-style-type: none"><li>Heavily dependant on caregivers resulting in very high disease burden</li></ul>	<ul style="list-style-type: none"><li>No available therapy</li><li>Easy diagnosis once considered with readily available, low-cost lab-test</li><li>Large proportion of patients remain undiagnosed with significant delay to diagnosis</li></ul> <div></div> <ul style="list-style-type: none"><li>Significant unmet medical need: humanitarian, health economic, societal</li></ul>	<table><tr><td><b>Median onset of symptoms:</b></td><td><b>4 months</b></td></tr><tr><td><b>Median age of diagnosis:</b></td><td><b>24 months</b></td></tr><tr><td><b>Patients surviving into adulthood:</b></td><td><b>70%</b></td></tr><tr><td><b>Severe intellectual disability:</b></td><td><b>100%</b></td></tr><tr><td><b>Ability to sit independently:</b></td><td><b>8%</b></td></tr><tr><td><b>Hypotonia, hypertonia &amp; persistence of primitive reflexes:</b></td><td><b>90%</b></td></tr><tr><td><b>Severe underweight:</b></td><td><b>75%</b></td></tr><tr><td><b>Cardiac arrythmias (PAC):</b></td><td><b>76%</b></td></tr><tr><td><b>Median life expectancy:</b></td><td><b>35 years</b></td></tr><tr><td><b>Life long 24-hour care:</b></td><td><b>100%</b></td></tr></table>	<b>Median onset of symptoms:</b>	<b>4 months</b>	<b>Median age of diagnosis:</b>	<b>24 months</b>	<b>Patients surviving into adulthood:</b>	<b>70%</b>	<b>Severe intellectual disability:</b>	<b>100%</b>	<b>Ability to sit independently:</b>	<b>8%</b>	<b>Hypotonia, hypertonia &amp; persistence of primitive reflexes:</b>	<b>90%</b>	<b>Severe underweight:</b>	<b>75%</b>	<b>Cardiac arrythmias (PAC):</b>	<b>76%</b>	<b>Median life expectancy:</b>	<b>35 years</b>	<b>Life long 24-hour care:</b>	<b>100%</b>
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Note: 1) Picture from Schwarz et al; Clin Endocrinol & Met 2007; 2) Groeneweg et al, Lancet Diabetes & Endocrinology, 2020

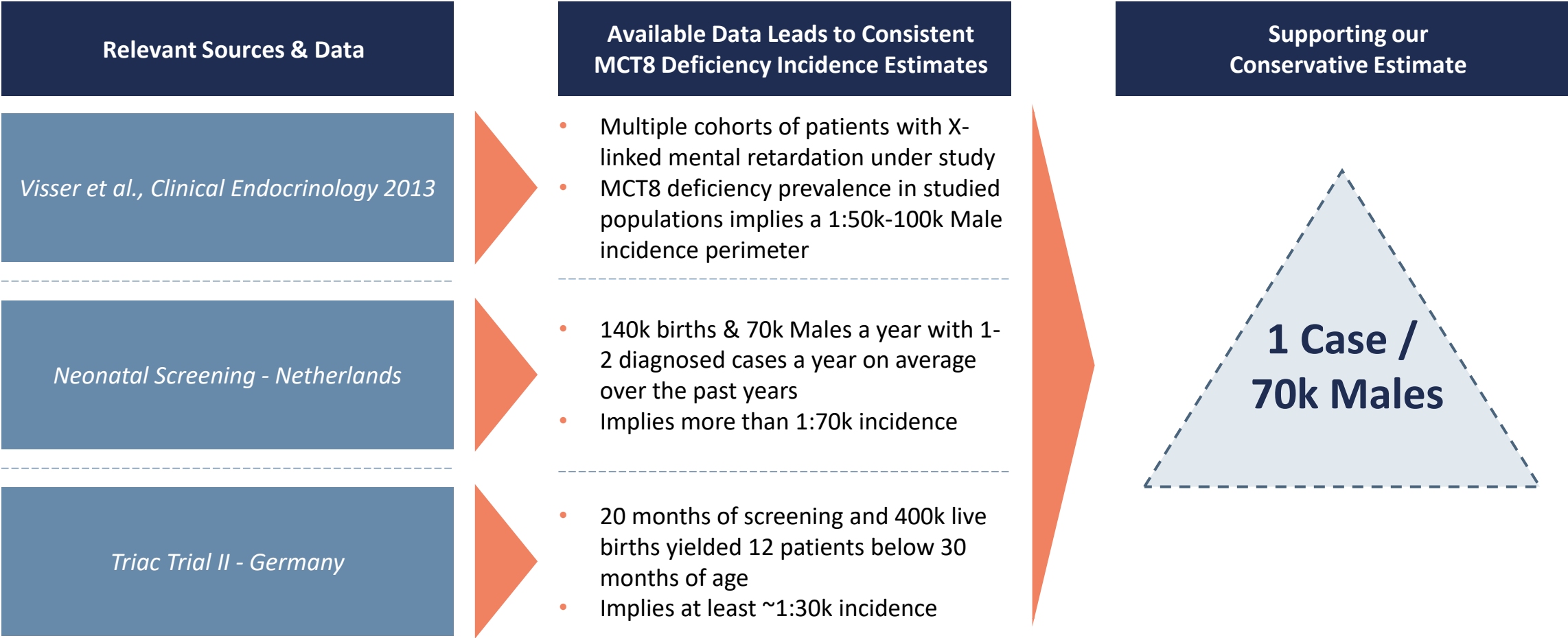
# Natural history study revealed poor survival with a high prevalence of treatable underlying risk factors

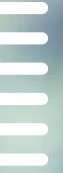
*An international, retrospective, multicentre cohort study from 2014-2020 in 151 patients*

- 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





## 2.

### *Clinical experience with Emcitate*

# Orphan drug candidate

*with clear scientific and mechanistic rationale and established safety profile*

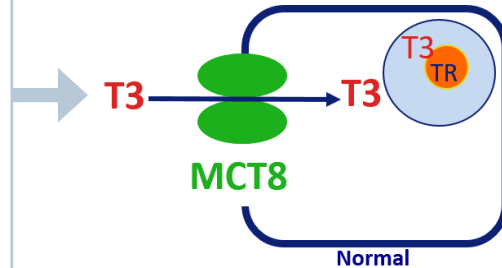


## Difference normal MCT8 and deficiency of MCT8

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

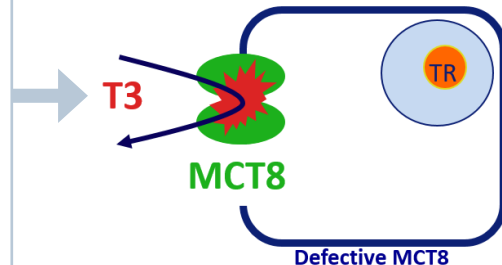
### Normal MCT8 ✓

- 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

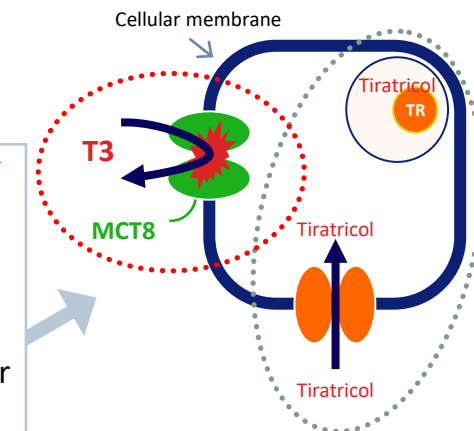


## Emcitate (tiratricol) – Addressing MCT8 deficiency

- 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
- Experience from 40 years on the French market in a different indication, owned and controlled by the company

### 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 ✓

# Emcitate® Overview

*Lead candidate for addressing MCT8 deficiency, a condition with high unmet medical need and no available treatment*



## Clinical

- **Triac Trial I** completed with significant and clinically relevant effects
- **Erasmus Medical Center cohort study confirms long-term efficacy and safety for up to 6 years (2021)**
- **Triac Trial II**, early intervention trial in young subjects to establish the effect on neurocognitive development, previously seen in Triac Trial I. Fully recruited Q2 2022, 22 patients. Results expected mid 2024

## Regulatory

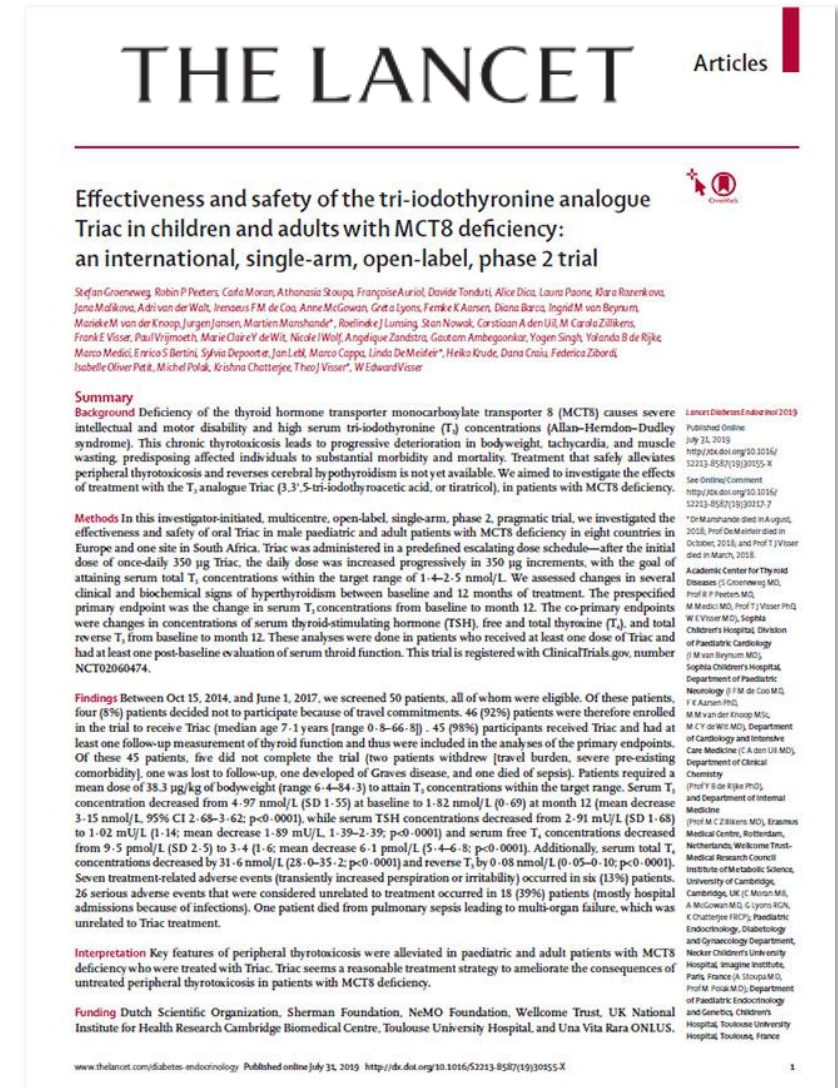
- Orphan drug designation in EU & US, US Rare Pediatric Disease Designation - **eligible for Priority Review Voucher**
- **Fast track designation** granted by FDA
- **Intend to submit MAA to the EMA based on existing clinical data early autumn 2023**
- **US NDA submission planned Q4 2023:** A 30-day, placebo-controlled study in 16 patients will be conducted to verify the results on T3 levels seen in previous clinical trials and publications

## Commercial

- Est. 10k – 15k MCT8 deficiency patients (1:70k males), no sponsor-initiated trials ongoing in MCT8 deficiency
- Analogue orphan drugs priced at premium
- **Launched disease awareness initiatives to support diagnosis of MCT8 deficiency**
- Around **180 patients** are being treated with Emcitate on an individual license or compassionate use basis, following individual regulatory approvals from national regulatory agencies
- Expected **market exclusivity** is **10y in EU (ODD)**, **7y in US (ODD)**

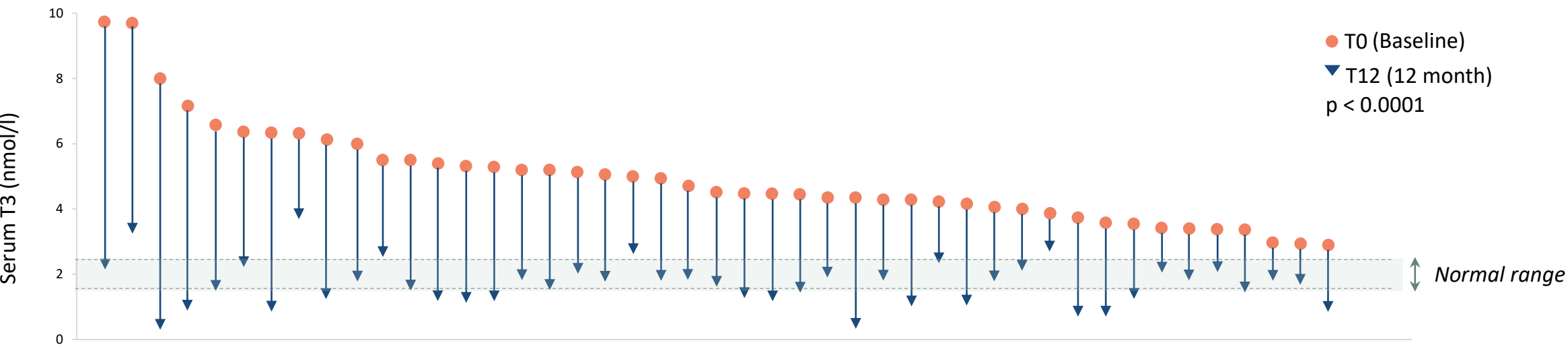
# Overview of completed Phase IIb – Triac Trial I

Primary objective and results	<ul style="list-style-type: none"><li>Evaluate the efficacy and safety of oral administration of tiratricol in male patients with MCT8 deficiency of all ages</li><li>Highly significant primary outcome - Change in T3 serum concentrations</li><li>Safe and tolerable</li><li>Results published in <i>The Lancet</i> 2019</li></ul>
Secondary objective and results	<ul style="list-style-type: none"><li>Change in other thyroid hormone function tests, thyrotoxic symptoms and markers</li><li>Significant and clinically relevant effects observed across secondary endpoints</li></ul>
Description	<ul style="list-style-type: none"><li>An international, single-arm, open-label, Phase II trial</li><li>ClinicalTrials.gov identifier: NCT02060474</li></ul>
# of patients	<ul style="list-style-type: none"><li>46 MCT8 patients in 9 countries</li></ul>
Timetable	<ul style="list-style-type: none"><li>Initiated in 2014 (first patient in)</li><li>Completed in 2018</li></ul>



# Consistent, clinically relevant and highly significant results

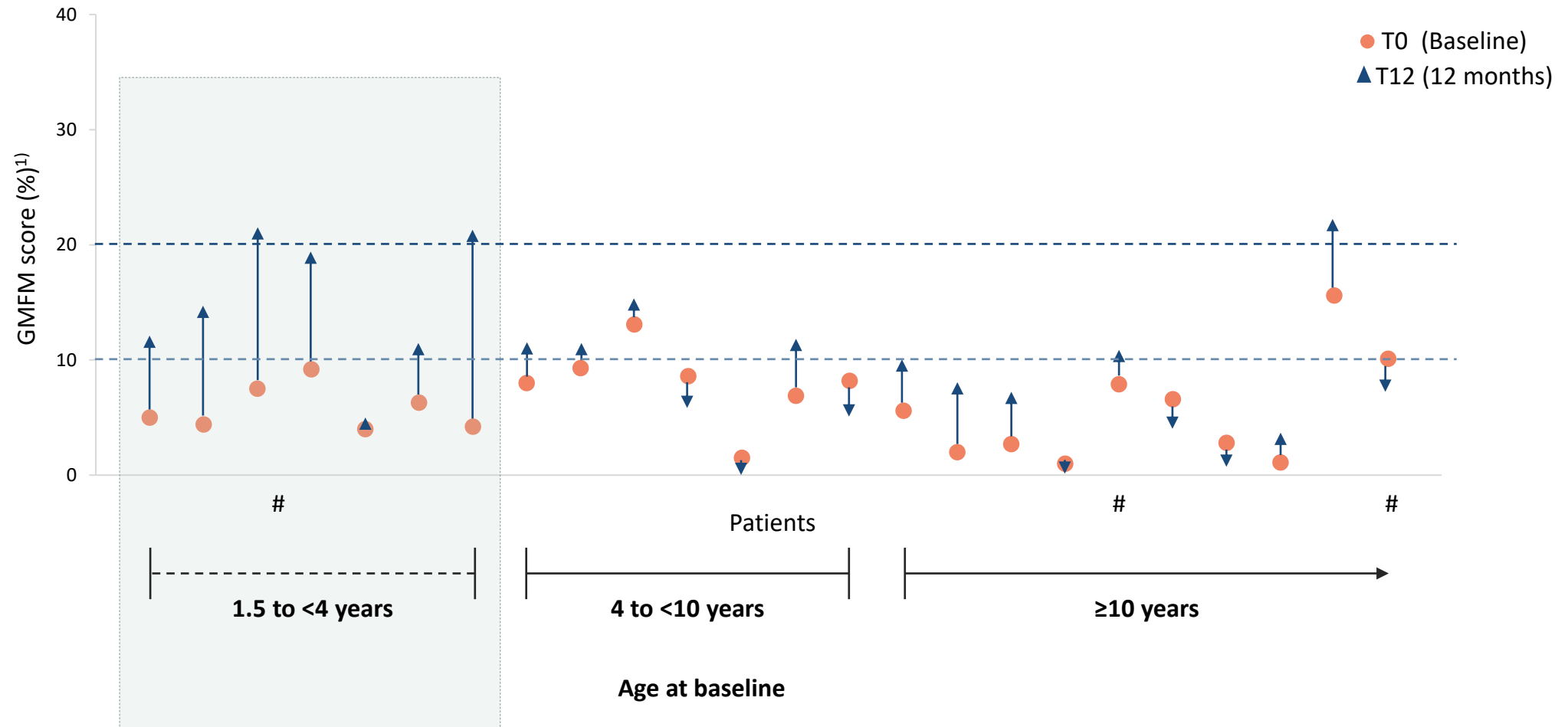
*Triac Trial I: Reached target level serum T3 & improvements in clinically relevant outcome measures*



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

# Triac Trial I: Indication of positive effect on neurocognitive development

*In the youngest patients which is further studied in ongoing, fully recruited, Triac Trial II*



# New data confirms 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](#)

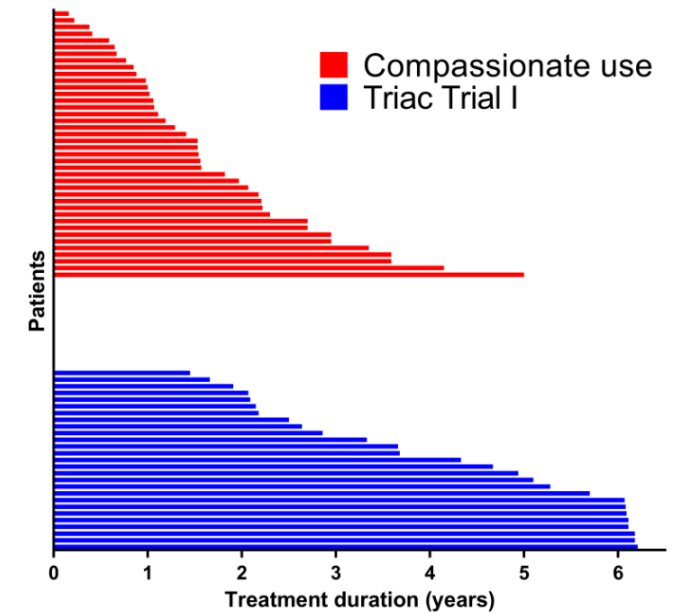
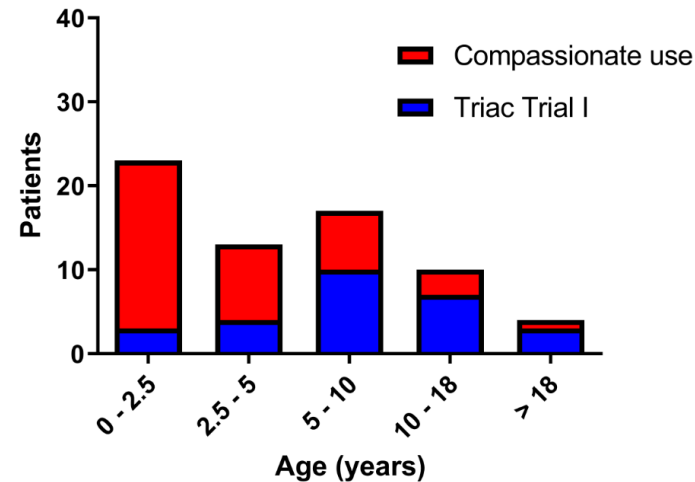
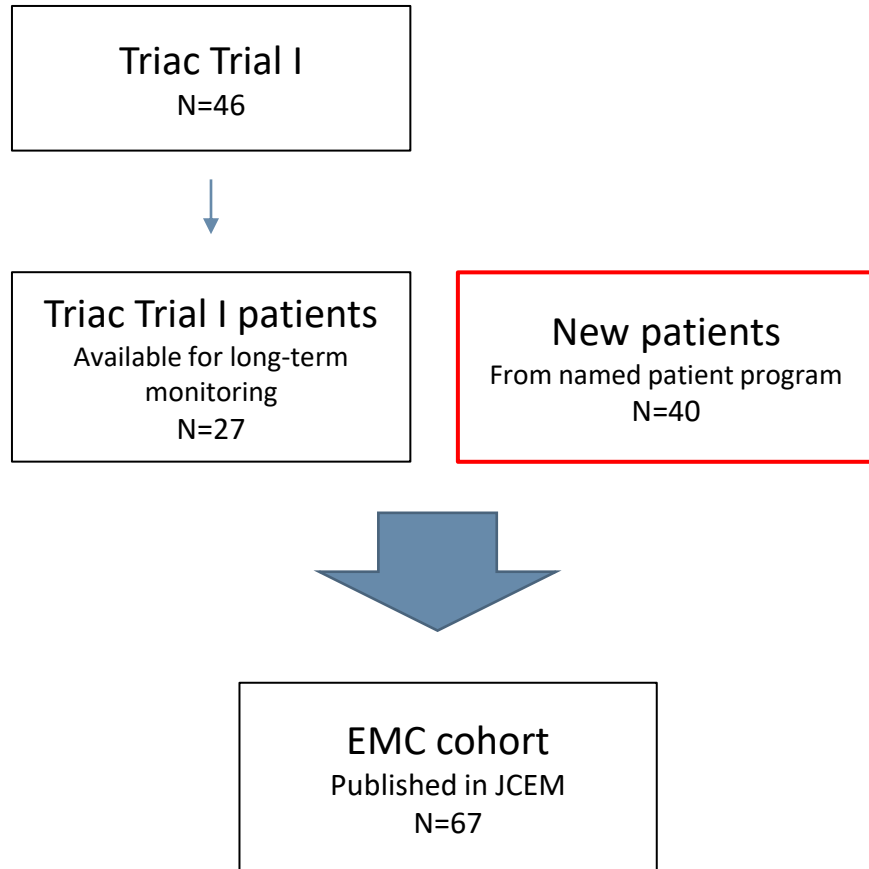
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- Investigator-initiated real-world cohort study at 33 sites conducted by the Erasmus Medical Center
- Investigated efficacy and safety of Emcitate in 67 patients with MCT8 deficiency
  - Median baseline age of 4.6 years (range: 0.5–66 years) and were 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

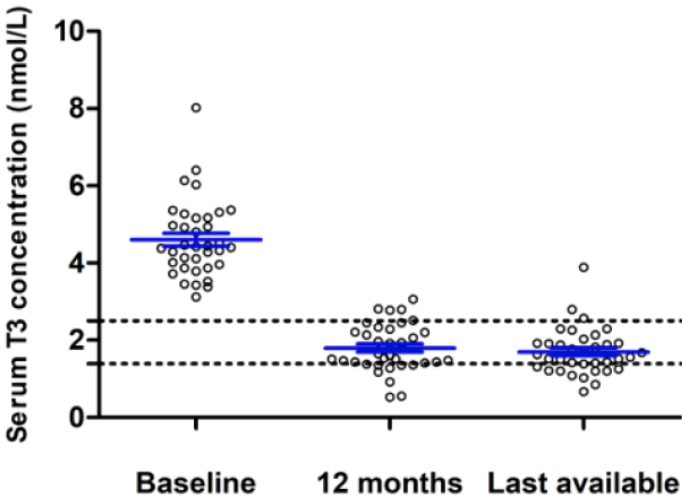
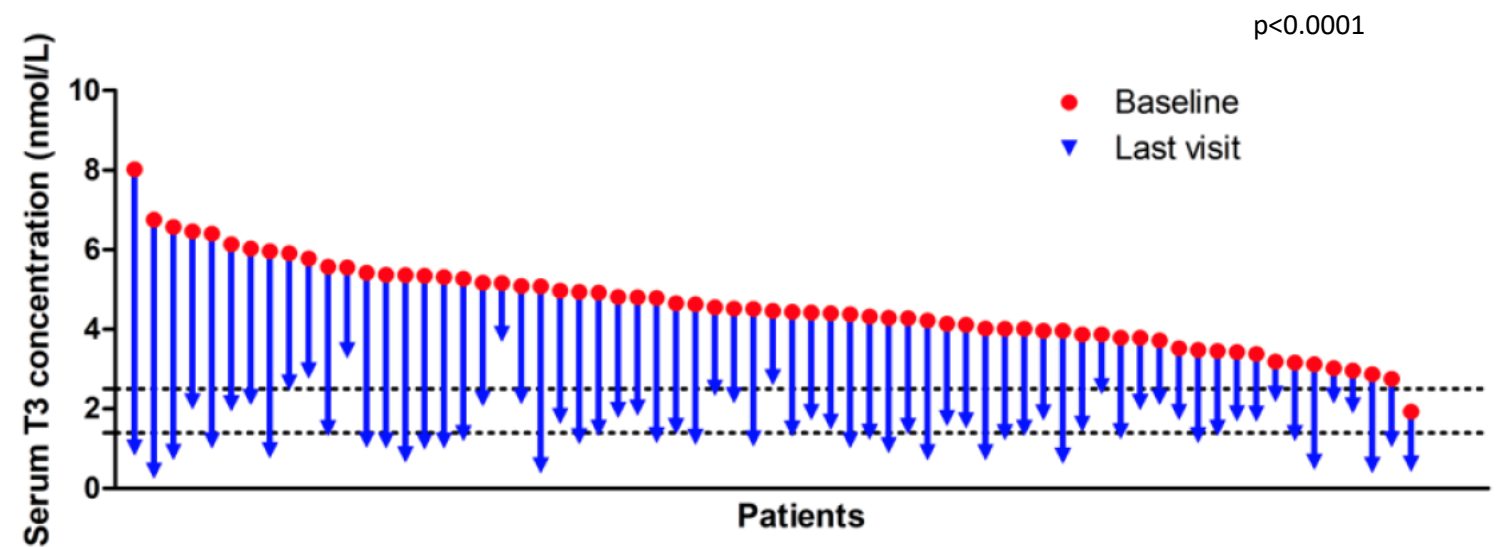
# New patient cohort of equal size to the Triac Trial I

*Long term follow up, up to >6 years*



# New cohort confirms primary endpoint results in Triac Trial I

*Fast and durable normalization of T3 values in almost all patients*

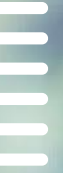


# Consistent, clinically relevant and highly significant results across endpoints

- 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
<b>Primary outcome</b>				
T3 (nmol/L; n=67)	4.58 (1.11)	1.66 (0.69)	-2.92 (-3.23 to -2.61)	<0.0001
<b>Secondary outcomes</b>				
<i>Anthropometric parameters and heart rate</i>				
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
<i>Thyroid function tests</i>				
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
<i>Peripheral markers</i>				
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).				



## 2.

*Emcitate<sup>®</sup> - regulatory pathway to submissions 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)

Fast  
track

**Fast track designation (FDA)**

**Eligibility:** Six months review of NDA & rolling submission

PRV

**Rare pediatric disease designation (FDA)**

**Eligibility:** Priority review voucher upon approval\*

MAA  
NDA

**MAA:** All clinical data available (submission early autumn '23)

**NDA:** Small confirmatory study agreed with FDA (submission Q4 '23)



ODD

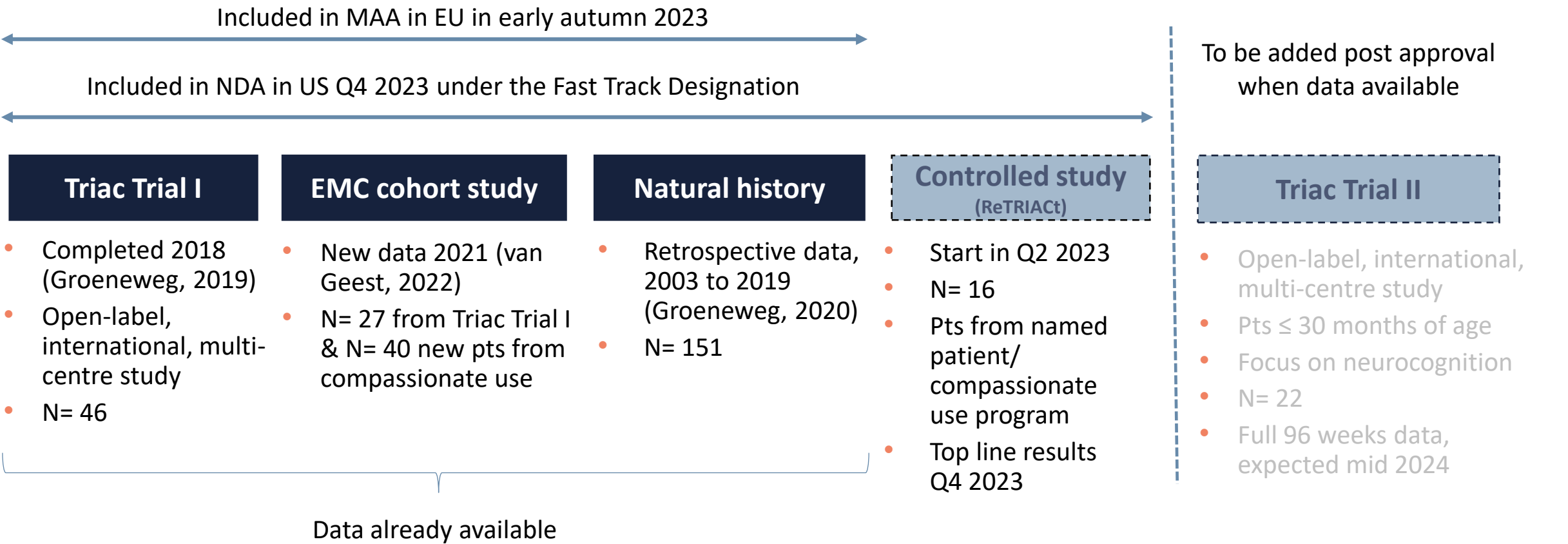
**Orphan drug designation for RTH-beta**

**Eligibility:** Market exclusivity for distinct indication

\*The voucher may be sold to another sponsor (2021-22 range: \$100m-\$110m)

# Emcitate regulatory pathway to submissions in EU and US

*The first potential treatment for MCT8 deficiency, a rare genetic disease with high unmet medical need and no available treatment*



# Egetis intends to submit MAA for Emcitate® to EMA in early autumn 2023 based on existing clinical data



- Based on regulatory interactions, Egetis concludes that **available data** from Triac Trial I and recently published long-term data are **sufficient for a Marketing Authorisation Application (MAA) in Europe**
- Having all clinical data required for regulatory submission already at hand **significantly reduces the remaining risk** for Emcitate
- The ongoing Triac Trial II will continue to further establish the effects of early intervention on the neurocognitive development aspects of the disease

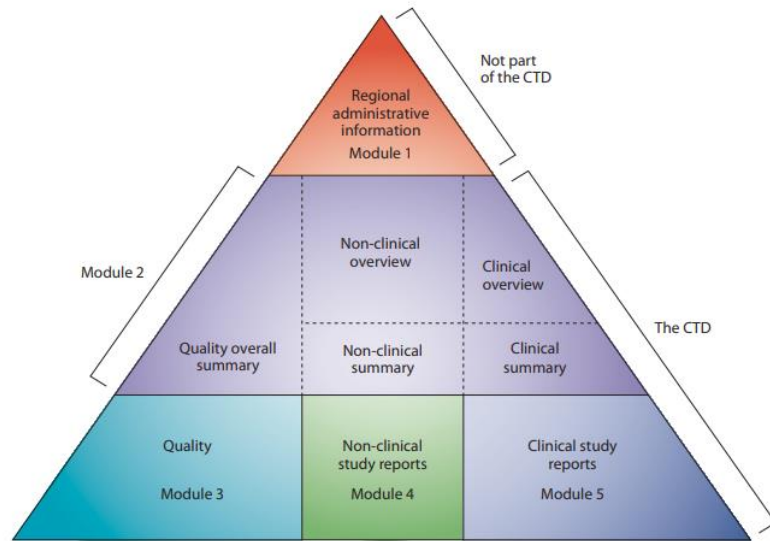
## Egetis intends to submit a marketing authorisation application for Emcitate® to the European Medicines Agency based on existing clinical data

- *Egetis concludes, based on recent regulatory interactions, that available Triac Trial I data together with recently published long-term data are sufficient for a Marketing Authorisation Application in Europe*
- *Having all clinical data required for regulatory submission already at hand significantly reduces the remaining risk for Emcitate*
- *Revised submission timelines will be communicated as soon as all parts of the regulatory dossier are confirmed*
- *Egetis will host a webcast today at 15:00 CET (9:00am ET)*

**Stockholm, Sweden, December 13, 2021** - Egetis Therapeutics AB (publ) (Nasdaq Stockholm: EGTX) today announced that after a pre-submission meeting held last week with concerned European regulatory agencies (EMA's Rapporteur and Co-Rapporteur), the Company concludes that the clinical data from the Triac Trial I (Groeneweg et al. 2019), together with the data from long-term treatment with Emcitate (tiratricol) for up to six years in 67 patients (van Geest et al. 2021) will be sufficient for a regulatory review of a Marketing Authorisation Application (MAA) to the European Medicines Agency for the treatment of monocarboxylate transporter 8 (MCT8) deficiency. Thus, all clinical data necessary for regulatory submission is already available. The ongoing Triac Trial II will continue to further establish the effects of early intervention on the neurocognitive development aspects of the disease.

*"We are delighted with the outcome of the pre-submission meeting, giving us a clear path to our MAA submission, and subsequent regulatory review, based on existing clinical data. Having all clinical data required for regulatory submission already at hand significantly reduces the remaining risk for Emcitate and could also potentially enable an earlier submission in Europe than we had previously expected. This is a substantial opportunity for us and the European patients suffering from MCT8 deficiency. In parallel, as part of our efforts to make Emcitate available as soon as possible, we continue our dialogues with regulatory authorities in other jurisdictions to obtain their views on the available clinical data and its implications for regulatory submissions" said Nicklas Westerholm, CEO, Egetis Therapeutics.*

# Content in *Emcitate* MAA submission



Common technical document

- Regulatory submissions in major regions contain the same type of key information on Efficacy, Safety and Quality
  - presented in a common format (called CTD - Common Technical Document)

## Key components of regulatory dossier

Clinical data



Non-clinical data



General items

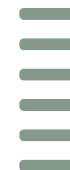


CMC\*

\*Pending stability data

CMC: Chemistry, manufacturing and controls

# Treatment effects on T3 levels in MCT8-deficiency could provide a basis for marketing approval in the US – NDA targeted in Q4 2023



- FDA acknowledges that a treatment effect on T3 levels and the manifestations of chronic thyrotoxicosis in MCT8-deficiency could provide a basis **for marketing approval** also in the US.
- A small, 30-day, placebo-controlled study in 16 treated patients, to be identified primarily through our existing named patient program, will be conducted to **verify the results on T3** levels seen in previous clinical trials and publications in a randomized **controlled** setting.
- An **NDA** in the US is targeted to be submitted in **Q4 2023** under the Fast Track Designation.
- A major step towards marketing authorization and increases the likelihood of success for *Emcitate* and the probability to receive a US Rare Pediatric Disease **Priority Review Voucher (PRV)**.

## Egetis concludes that demonstrating treatment effects on T3 levels in MCT8-deficiency could provide a basis for marketing approval for *Emcitate*® in the US

- *Emcitate*® (tiratricol) is the first potential treatment of MCT8 deficiency, a rare genetic disease with high unmet medical need and no available treatment
- In recent positive regulatory interactions, FDA acknowledges that a treatment effect on T3 levels and the manifestations of chronic thyrotoxicosis in MCT8-deficiency could provide a basis for marketing approval also in the US.
- An NDA in the US is targeted to be submitted in mid-2023 under the Fast Track Designation.
- A small, 30-day, placebo-controlled study in 16 treated patients, to be identified through the existing named patient program, will be conducted to verify the results on T3 levels seen in previous clinical trials and publications in a randomized controlled setting
- This is a major step towards a marketing application and increases the likelihood of success for *Emcitate* and the probability for Egetis to receive a US Rare Pediatric Disease Priority Review Voucher (PRV).
- Egetis will host a webcast today at 15:00 CET (9:00am ET)

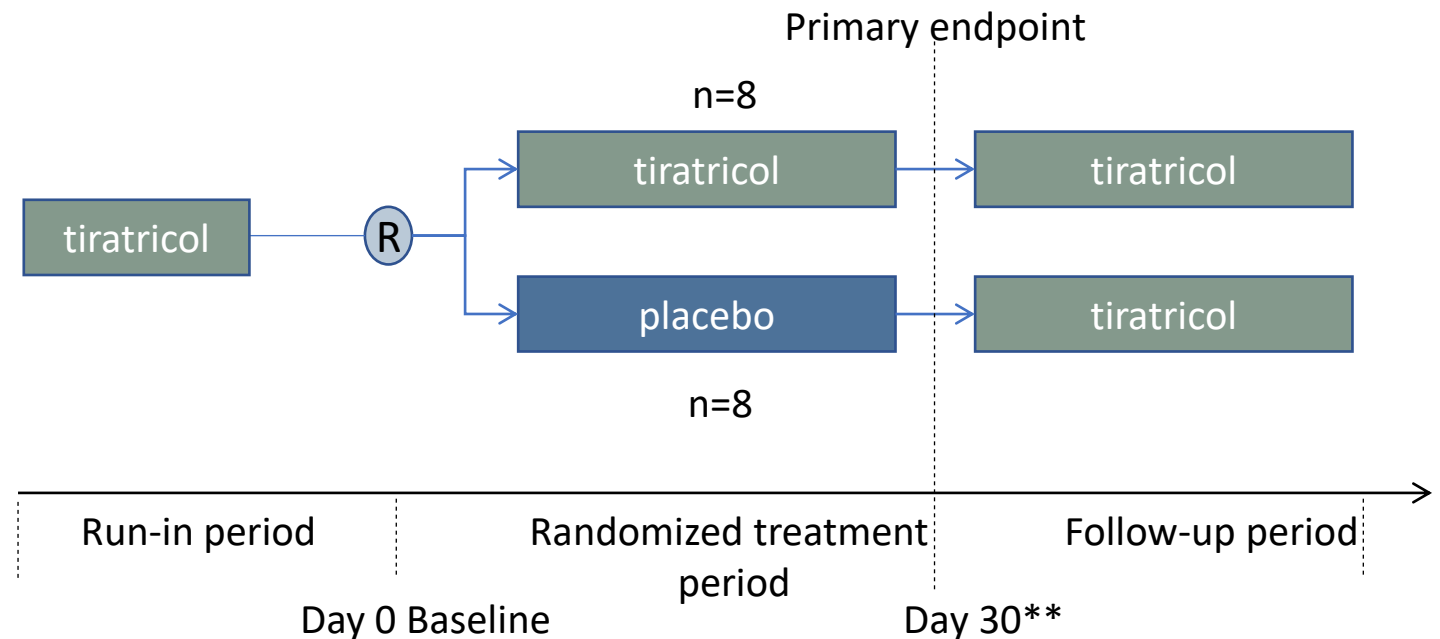
Stockholm, Sweden, January 18, 2022 - Egetis Therapeutics AB (publ) (Nasdaq Stockholm: EGTX) (the "Company") today announced that in recent regulatory interactions, the US Food and Drug Administration (FDA) acknowledges that demonstrating a treatment effect on thyroid hormone T3 levels and the manifestations of chronic thyrotoxicosis could provide a basis for marketing approval also in the US. Consequently, the Company now has an aligned regulatory strategy for EU and US. The Company intends to submit a New Drug Application (NDA) in the US for *Emcitate*® (tiratricol) for the treatment of monocarboxylate transporter 8 (MCT8) deficiency in mid-2023 under the Fast Track Designation granted by the FDA in October 2021. This follows the announcement in December 2021 of intention to submit the Marketing Authorisation Application (MAA) for *Emcitate* to the European Medicines Agency (EMA) based on existing clinical data on the manifestations of chronic thyrotoxicosis in MCT8 deficiency.

# ReTRIACt – Measuring proportion of patients meeting $T3 \geq ULN$ within the randomized treatment period

*Randomised placebo controlled study to verify previous single arm Triac I trial and real-world cohort study results*

- FDA acknowledges that a treatment effect on T3 levels and the manifestations of chronic thyrotoxicosis in MCT8-deficiency could provide a basis **for marketing approval** also in the US.
- A small, 30-day, placebo-controlled study in 16 treated patients, to be identified primarily through our existing named patient program, will be conducted to **verify the results on T3** levels seen in previous clinical trials and publications in a randomized **controlled** setting.
- An **NDA** in the US is targeted to be submitted in **Q4 2023** under the Fast Track Designation.
- A major step towards marketing authorization and increases the likelihood of success for *Emcitate* and the probability to receive a US Rare Pediatric Disease **Priority Review Voucher (PRV)**.

## Controlled Study (ReTRIACt) – design agreed with FDA



**Primary endpoint: Proportion of participants who meet the rescue criterion ( $T3 > ULN$ ) during the 30-day double-blind Randomized Treatment Period**

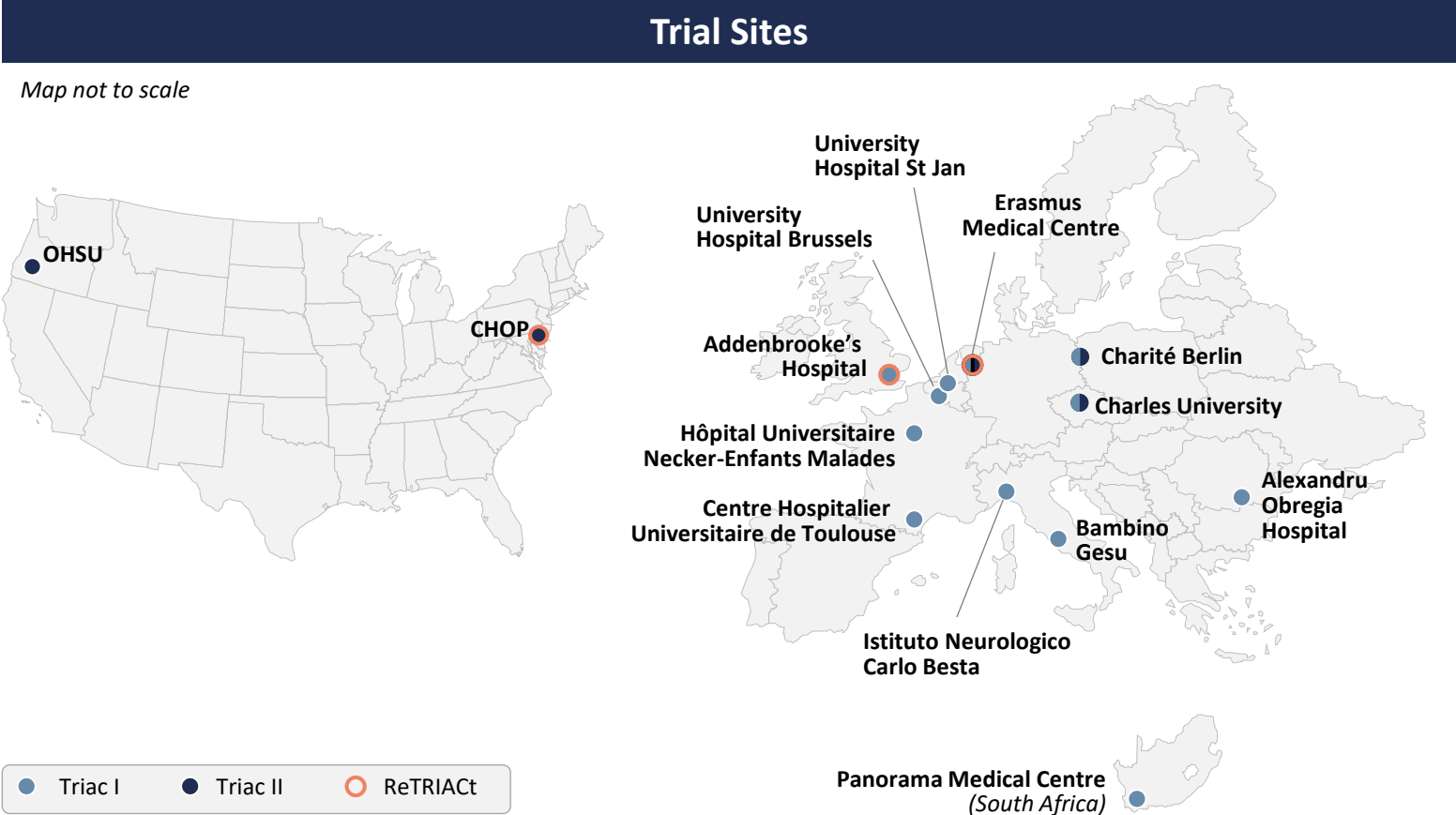
\* ULN: Upper Limit of Normal

\*\* Randomized treatment period ends after 30 days or when rescue criterion ( $T3 > ULN$ ) is met, whichever comes first

# ReTRIACt: withdrawal of *Emcitate* in males with MCT8 deficiency

Randomized placebo-controlled trial needed for NDA submission

Primary Endpoint	<ul style="list-style-type: none"><li>Proportion of participants who meet the rescue criterion (serum total T3 &gt; ULN) during the 30-day double-blind Randomized Treatment Period</li></ul>
Secondary Endpoints	<ul style="list-style-type: none"><li>Change in cardiovascular variables</li><li>Change in serum thyroid hormone variables</li></ul>
Description	<ul style="list-style-type: none"><li>Double-blind, randomized, multi-center placebo-controlled study</li><li>Participants with stable maintenance treatment with <i>Emcitate</i></li><li>Design agreed with FDA</li><li>Clinicaltrials.gov identifier: NCT05579327</li></ul>
# of Patients	<ul style="list-style-type: none"><li>16 patients, &gt; 4 years of age</li><li>Primary source of patients from NPU program</li></ul>
Timetable	<ul style="list-style-type: none"><li>Study to start Q2 2023</li><li>Completion expected in Q4 2023</li></ul>



**All 3 sites in ReTRIACt used in prior Triac Trial I and/or ongoing Triac Trial II**

**Triac I study sites include:** Addenbrooke's Hospital (Cambridge, UK), Alexandru Obregia Hospital (Bucharest, Romania), Bambino Gesù (Rome, Italy), Centre Hospitalier Universitaire de Toulouse (Toulouse, France), Charité Berlin (Berlin, Germany), Charles University (Prague, Czech Republic), Erasmus Medical Centre (Rotterdam, Netherlands), Hôpital Universitaire Necker-Enfants Malades (Paris, France), Istituto Neurologico Carlo Besta (Milan, Italy), Panorama Medical Centre (Panorama, South Africa), University Hospital Brussels (Brussels, Belgium) and University Hospital St Jan (Brugge, Belgium).

**Triac II study sites include:** Children's Hospital of Philadelphia (Philadelphia, Pennsylvania), Charité Berlin (Berlin, Germany), Charles University (Prague, Czech Republic), Erasmus Medical Centre (Rotterdam, Netherlands) and OHSU (Portland, Oregon).

**ReTRIACt study sites include:** Addenbrooke's Hospital (Cambridge, UK), Children's Hospital of Philadelphia (Philadelphia, Pennsylvania) and Erasmus Medical Centre (Rotterdam, Netherlands).

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

*Randomized placebo-controlled trial needed for NDA submission*



Primary endpoint	<ul style="list-style-type: none"><li>• Proportion of participants who meet the rescue criterion (serum total T3 &gt; ULN) during the 30-day double-blind Randomized Treatment Period</li></ul>
Secondary endpoints	<ul style="list-style-type: none"><li>• Change in cardiovascular variables</li><li>• Change in serum thyroid hormone variables</li></ul>
Description	<ul style="list-style-type: none"><li>• Double-blind, randomized, multicenter placebo-controlled study</li><li>• Participants with stable maintenance treatment with <i>Emcitate</i></li><li>• Design agreed with FDA</li><li>• Clinicaltrials.gov identifier: NCT05579327</li></ul>
# of patients	<ul style="list-style-type: none"><li>• 16 patients, &gt; 4 years of age</li><li>• Primary source of patients from NPU program</li></ul>
Timetable	<ul style="list-style-type: none"><li>• Study to start Q2 2023</li><li>• Completion expected in Q4 2023</li></ul>



# Triac Trial II fully recruited: to establish effects of early intervention on neurocognitive development

*Market approval not dependent on Triac Trial II data*

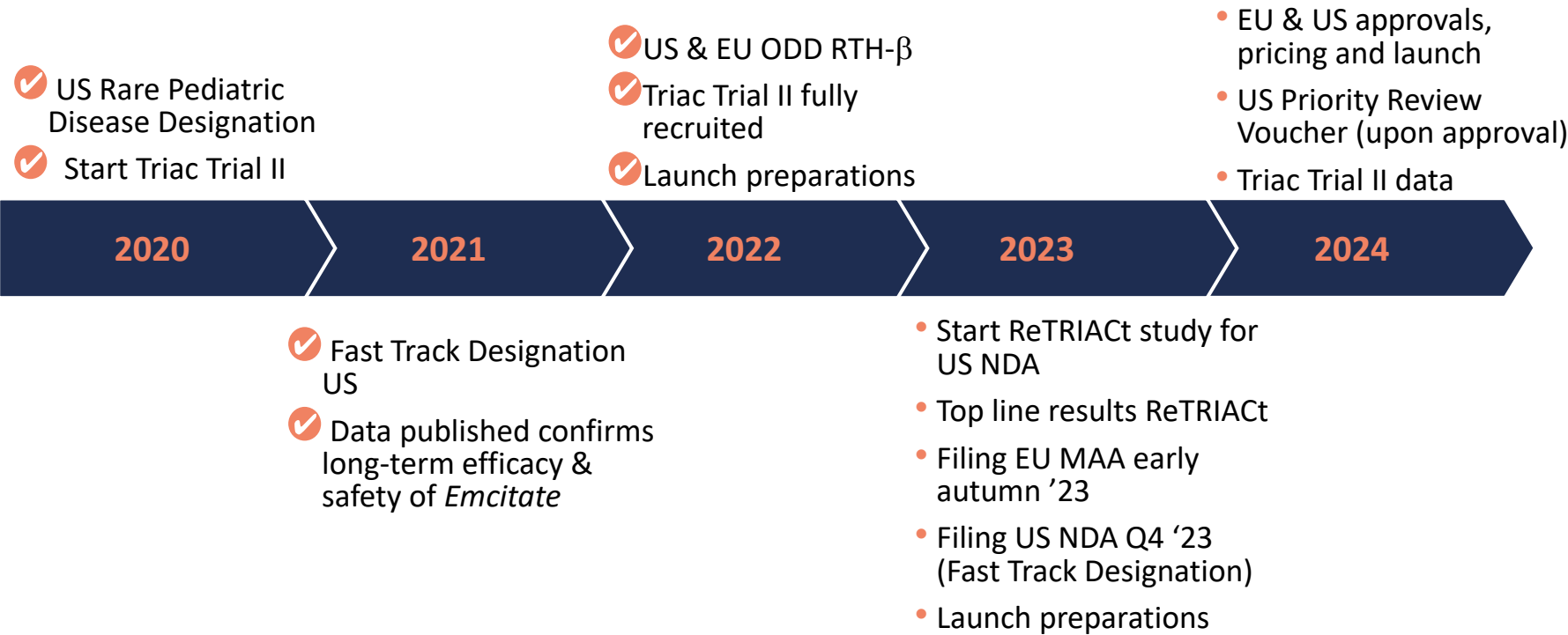


Primary Objective	<ul style="list-style-type: none"><li>• Confirm findings from Triac Trial I in youngest age group</li><li>• Improvement in neurocognitive development as measured by GMFM<sup>1</sup> and BSID-III<sup>2</sup> compared to natural history controls</li></ul>
Secondary Objective	<ul style="list-style-type: none"><li>• Achievement of motor milestones (e.g. hold head, sit independently)</li><li>• Normalization of thyroid hormone function tests and markers of thyrotoxicosis</li></ul>
Description	<ul style="list-style-type: none"><li>• Open label, multi-centre trial in very young children with MCT8 deficiency</li><li>• International trial with 10 centres in CZ, DE, IT, UK, FR, NL, US</li><li>• Design discussed and anchored with EMA and FDA</li><li>• ClinicalTrials.gov identifier: NCT02396459</li></ul>
# of Patients	<ul style="list-style-type: none"><li>• 22 children, 0-30 months of age</li></ul>
Timetable	<ul style="list-style-type: none"><li>• First Patient First Visit in Dec 2020, recruitment target met in April 2022</li><li>• Results from 96 week read out expected mid 2024 and data is expected to be submitted post-approval to regulatory authorities shortly thereafter and available for HTA interactions</li><li>• Market approval not dependent on Triac Trial II data</li></ul>



1. Gross motor function measure.  
2. Bayley Scales of Infant Development.

# Emcitate milestones and timelines



# FDA granted Rare Pediatric Disease designation to Emcitate®

*US Rare Pediatric Disease Priority Review Voucher (PRV) provides a ~\$100m opportunity*

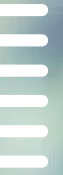


## Overview PRV

- 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 a US Rare Pediatric Disease Priority Review Voucher (PRV) upon approval.
- PRV program recently prolonged until 2026.
- 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 2021-22 8 PRVs for rare pediatric diseases have been sold, with individual voucher sale prices ranging from \$100m-\$110m.

## Examples of PRVs sold

Seller	Buyer	Value	Year
Liminal Biosciences	Undisclosed	\$105M	2021
Mirum Pharmaceuticals	Undisclosed	\$110M	2021
Rhythm Pharmaceuticals	Undisclosed	\$100M	2021
Albireo	Undisclosed	\$105M	2021
Biomarin	Undisclosed	\$110M	2022
BridgeBio	Undisclosed	\$110M	2022
Mallinckrodt	Novartis	\$100M	2022
Marinus Pharmaceuticals	Novo Nordisk	\$110M	2022

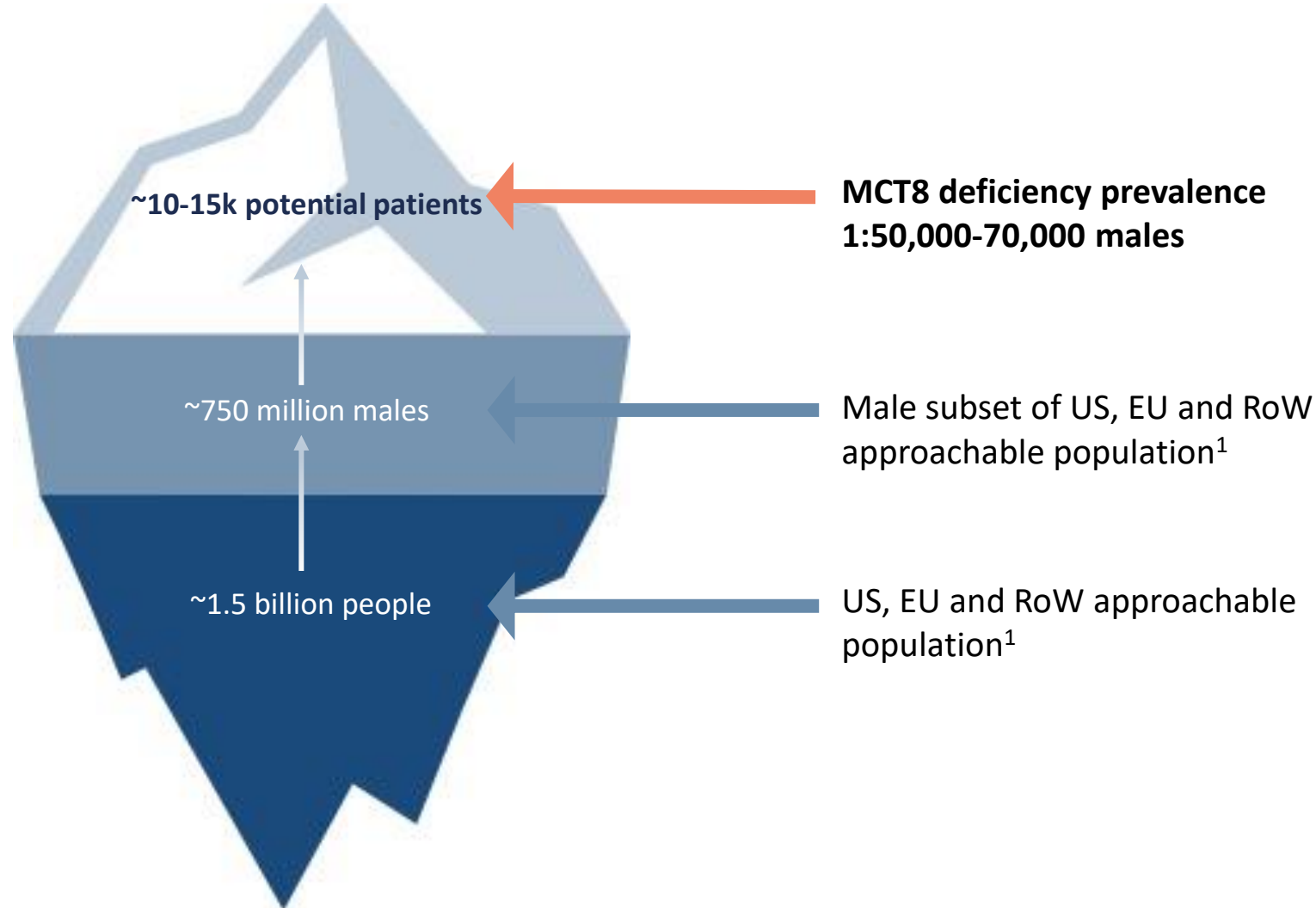


2.

*Emcitate<sup>®</sup> - Commercial opportunity*

# Estimating 10-15k addressable patients globally

*No approved treatment for MCT8 deficiency*



## MCT8 deficiency epidemiology

- At least one new-born diagnosed per 140,000 live births in the Netherlands in past years, corresponding to 1:70,000 males
- Actual number of patients could be higher:
  - Screening study suggests prevalence of 1:50,000 males<sup>2</sup>
  - Once treatment is available, more patients tend to be diagnosed

# Emcite<sup>®</sup> – 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<sup>1</sup>
- 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<sup>2</sup>

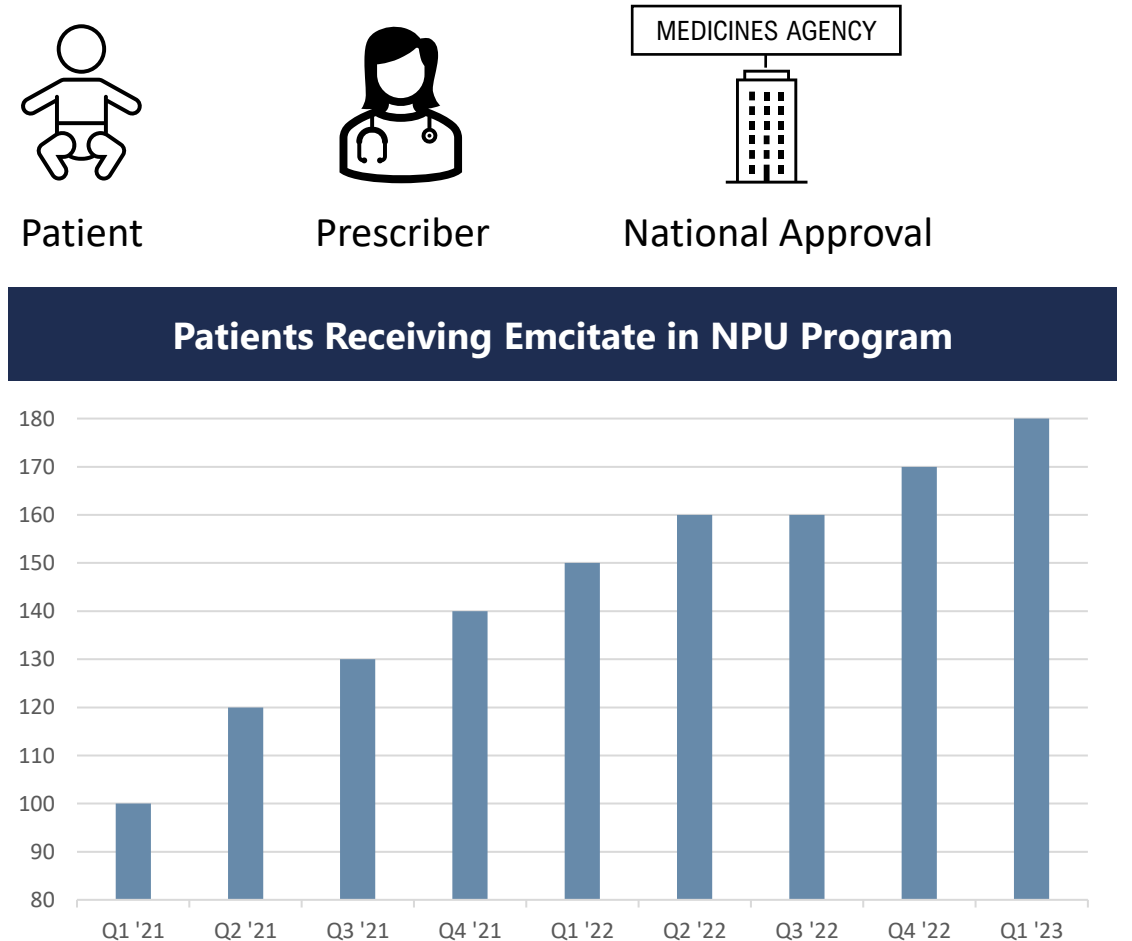


**Emcite** holds potential to become the **first approved therapy** to address the root cause of MCT8 deficiency, restore thyroid hormone signaling and thereby **prevent disease progression**, alleviate symptoms and **prolong lives**

# Emcitate supplied globally on a named patient basis

*The named patient use (NPU) confirms the significant unmet medical need in MCT8 deficiency and the view on how Emcitate address it*

- NPU and compassionate use 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
- Implemented Expanded Access Program as requested by the FDA - will Simplify Process for Accessing Emcitate
- Emcitate is being supplied on a named patient basis, following individual approval from the national medicines agencies, to
  - around 180 patients
  - in over 25 countries



# Commercialization of *Emcitate*

*Disease area conditions provide opportunity for lean commercialization*



## 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



## Stepwise establishing inhouse commercial capabilities

- Preparing for **2024 launch** in US and Europe with organization of **40-50** employees at time of launch
- Aiming for rapid access to *Emcitate* for all **MCT8 deficiency patients**:

**US: 2400\* patients**

**Europe: 5400\* patients**



Plan to commercialize in rest of world through partners

\*Based on prevalence 1:70,000 males

# Building commercial organization 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**

*– Leadership team brings launch skills and best practices from in total 100+ years at international companies*



Henrik Krook, SE  
VP Commercial Operations



Anny Bedard, US  
President Egetis North America



Marianne Berrens-Peijnenburg, NL  
Global Head  
Medical Affairs



Nigel Nicholls, UK  
GM for UK & Northern Europe



Nadia Georges, CH  
Global Head  
Market Access & Pricing



Raymond Francot, CH  
GM for DE, AT, CH &  
Central & Eastern Europe



Peter Verwaijen, NL  
Global Head  
Marketing & Brand Strategy



John Walsh, US  
VP Medical Affairs North America



# 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



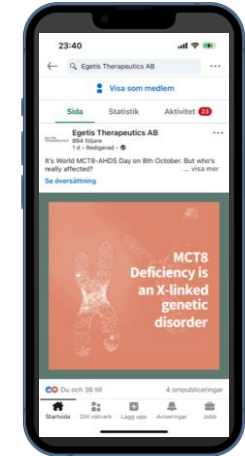
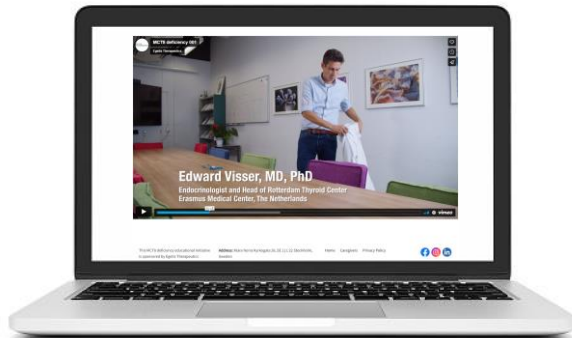
\*Emcitate promotion will start at the time of marketing authorization (in line with legislations). Before that, external initiatives are focused on MCT8 deficiency.

# Enabling patient identification through disease awareness

*MCT8 deficiency awareness and educational activities launched through various channels*



[mct8deficiency.com](https://mct8deficiency.com)



## DISEASE AWARENESS AND EDUCATION

- Focus on enabling early and accurate diagnosis
- ↑ number of physicians who
  - Are aware of MCT8 deficiency
  - Can diagnose
  - Understands how to manage MCT8 deficiency

## COLLABORATION WITH PAGs & KOLs

- KOL engagements and peer-to-peer education through national specialist societies
- International & national patient advocacy groups



## EXHIBIT AT SCIENTIFIC/MEDICAL CONFERENCES

- Euro Paediatric Neuro. Society
- European Thyroid Association
- European Society of Paediatric Endocrinology
- International Child Neurology Congress
- American Thyroid Association
- And more...

## OPTIMUM CHANNEL MIX FOR MAXIMUM REACH

- MCT8deficiency.com
- Instagram and Facebook
- Mailing campaigns to HCPs
- Social media and video for MCT8-AHDS day (Oct 8<sup>th</sup>)
- Congresses and F2F interactions
- Publications

# Aiming for broad access to Emcitate for affected families

*Payer projects initiated to generate optimal reimbursed price*

*– No families should pay out of own pocket*

- Payers in general **accept higher prices** for orphan drugs compared to traditional drugs and especially if they;

- Address an **ultra-rare** disease, e.g. prevalence less than 1:50,000 people
- Target a **severe** disease, i.e. life threatening/debilitating

- **Emcitate** fulfills these criteria, no other drugs available or being developed for MCT8 deficiency



1:70,000 males & even more rare in females



Severe impact on QoL, median survival 35y

## The pricing & reimbursement work has started

1. VALUE IDENTIFICATION, POSITIONING & EVIDENCE  
GENERATION

2. PRICE STRATEGY IMPLEMENTATION  
& VALUE COMMUNICATION

*Aiming for that Emcitate as soon as possible after marketing authorization is financed through country specific reimbursement mechanisms and that no family would have to pay for treatment out of own pocket*

# Developing a compelling Emcitate clinical and economic value proposition to secure reimbursement & access

*Key for payer assessments to describe unmet need & quantify burden of MCT8 deficiency*

- The **impact of MCT8 deficiency** on patients and caregivers is underreported
- Significant **clinical and economic burden**, both direct and indirect, which will be described and quantified
- Currently **generating data** for payers to answer the question “*What is the burden of MCT8 deficiency for patients & their caregivers?*”
  - **Vignette study** – Involving treating physicians to derive utility values for a defined range of MCT8 deficiency health states, suitable for cost-effectiveness analysis
  - **Caregiver study** – Generate burden of disease data (costs & QoL) from caregivers

## Example of Caregiver burden of disease publication in CLN2

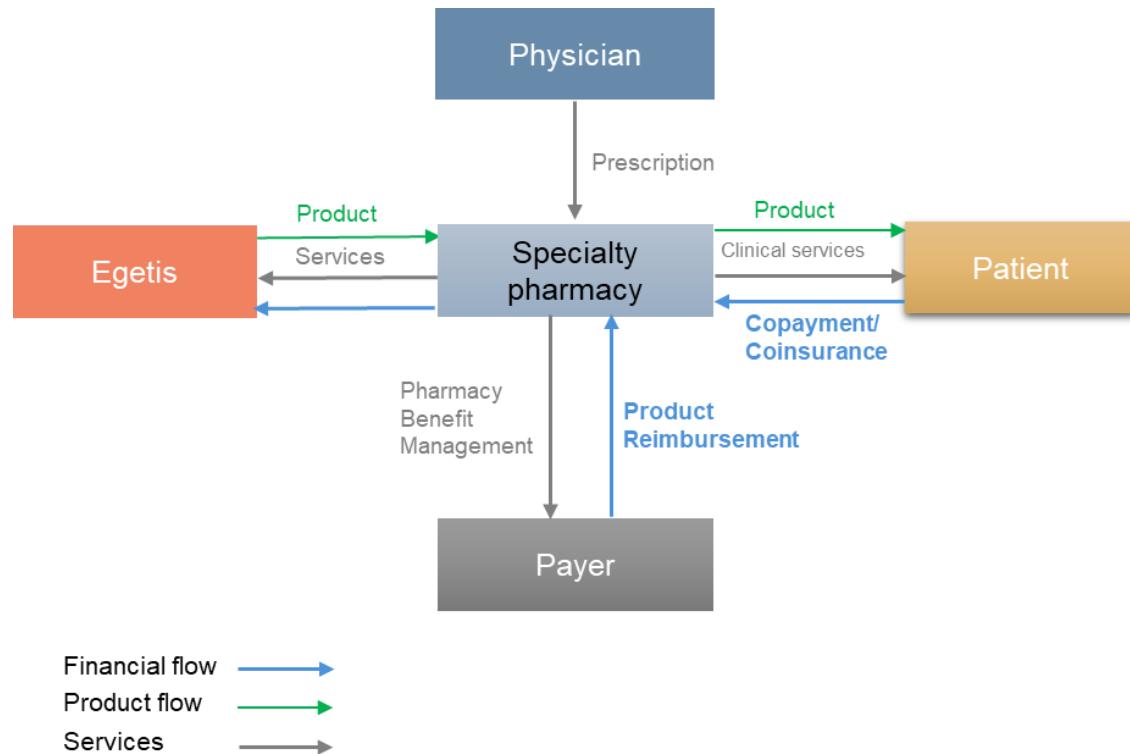


# Implemented Expanded Access Program as requested by the FDA - will Simplify Process for Accessing Emcitate



- High demand for single patient INDs (Investigational New Drug) resulting in process delays
- FDA Requested Expanded Access Program Transition - Simplify Process for Accessing Emcitate
- Patient Advocacy efforts focused on educating important stakeholders
- Incorporate the patient voice

# Exclusive Distribution Model Through Speciality Pharmacy is Preferred option for Rare Disease



- Insurance resolution and contracting
- Prior authorization support
- Appeals
- Dedicated case managers
- Improves patient experience and outcomes
- Patient Assistance and Copay Support
  - Aim for no family to pay out of pocket

# US Pricing & Reimbursement

Relatively straight forward for ultra-orphans with key focus on rarity and severity of disease

## Analogues selected based on:

- Rarity (ultra-orphan)
- Paediatric
- No treatment options
- Life-long treatment
- Disease severity

## Emcitate’s value drivers confirmed by US payer research:

*“You have all the things here: **terrible condition, ultra rare, deteriorating cognition, etc**”*

Chief Medical Officer  
Commercial Payer

*“The product gets paid for because they are **kids** and they need outcomes”*

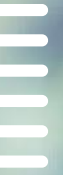
Medical Director  
Paediatrician  
Medicaid

*“If **FDA approves** this treatment, **we will cover it.**”*

Medical Director,  
Paediatrician  
Medicaid

## US Payer Analogues

	Exondys® <i>anti-sense oligonucleotide</i>	Ravicti® <i>Small molecule</i>	Oxlumo® <i>iRNA</i>	Brineura® <i>Recombinant enzyme</i>
Disease	Duchenne Muscular Dystrophy (13% of population)	Urea Cycle Disorders	Primary Hyperoxaluria	CLN2
Rarity - less than 1:50,000 people	✓	✓	✓	✓
Severity – life threatening/debilitating	✓	✓	✓	✓
US gross annual treatment cost	\$750k	\$750k	\$500k	\$750k



### 3.

*Paracetamol/Acetaminophen overdose and clinical experience with Aladote*

# 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

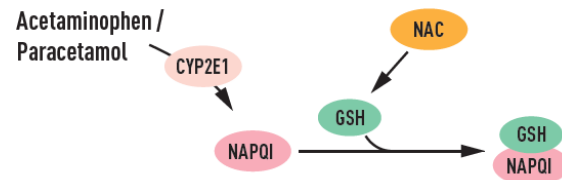
# Orphan drug candidate

*with clear scientific and mechanistic rationale*

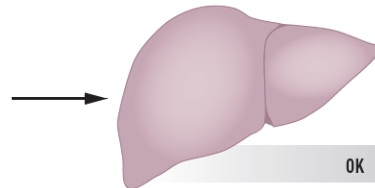
## Early presenters (<8h)

**NAC treatment effective against liver injury**

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



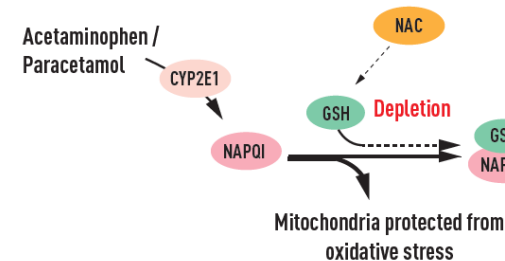
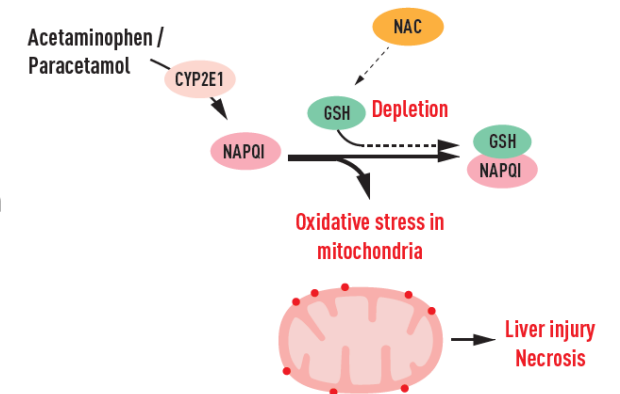
- In most cases NAC effectively prevents liver injury i.e. limited need for Aladote®



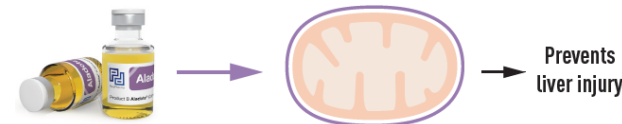
## Late presenters (>8h) are at increased-risk for liver injury

**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)**

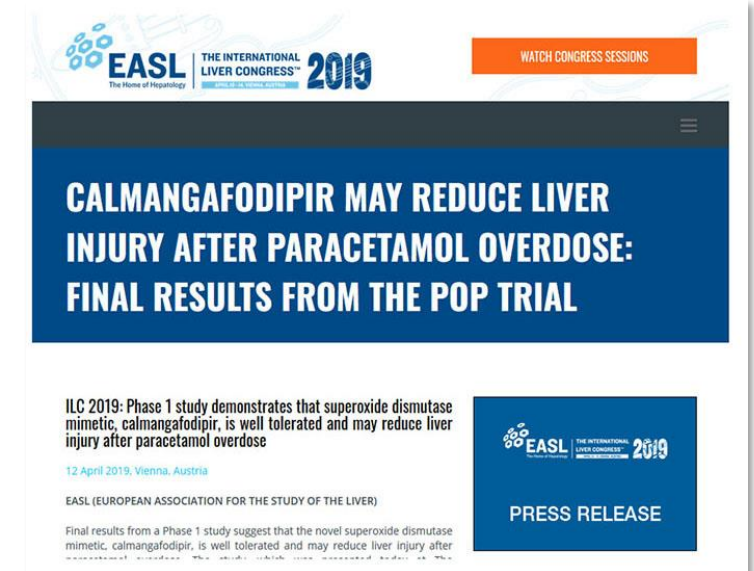


- Aladote®** (calmangafodipir) prevents ROS and RNS formation, restores mitochondrial energy production and **prevents liver injury**



# Overview of completed Phase Ib/IIa

Primary objective and results	<ul style="list-style-type: none"> <li>Met primary endpoint of safety tolerability in the combination of Aladote® and NAC</li> <li>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</li> <li>Presented at, American College of Medical Toxicology (ACMT) and Society of Toxicology (SOT), as novel emerging treatments for acetaminophen/paracetamol toxicity in 2021</li> </ul>
Secondary objectives and results	<ul style="list-style-type: none"> <li>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</li> </ul>
Description	<ul style="list-style-type: none"> <li>An open label, rising-dose, randomized study exploring safety and tolerability of Aladote® co-treatment with NAC</li> <li>ClinicalTrials.gov identifier: NCT03177395</li> </ul>
# of patients	<ul style="list-style-type: none"> <li>Single ascending dose study in 3 dosing cohorts of 8 patients (N=24) as add-on to NAC regime</li> </ul>
Timetable	<ul style="list-style-type: none"> <li>Initiated in June 2017 (first patient in)</li> <li>Completed in September 2018</li> </ul>



# 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%)

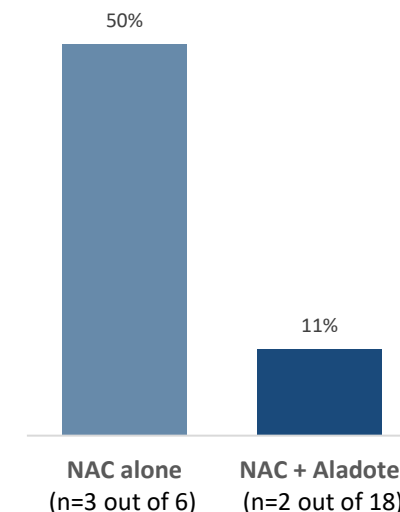
- Met primary endpoint of safety tolerability in the combination of Aladote® and NAC
- No AE or SAE probably or definitely related to Aladote®

## Liver injury – ALT<sup>1</sup> 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

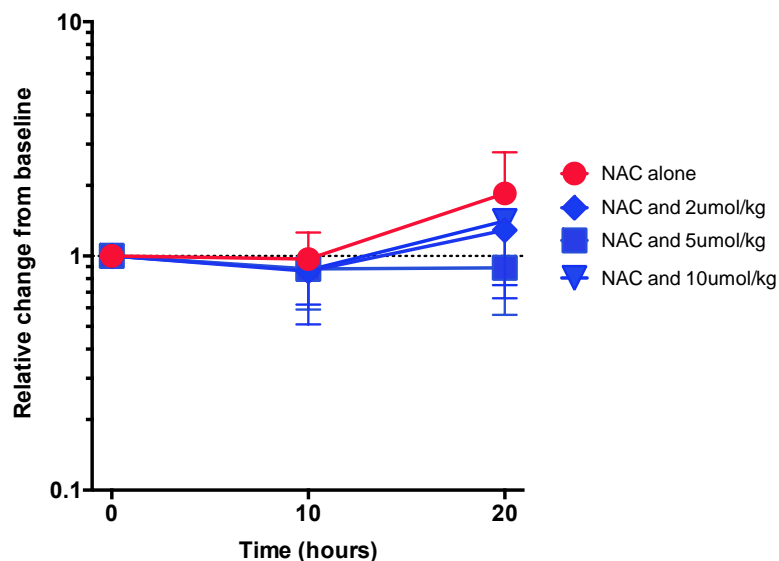


Note: (1) Alanine transaminase (ALT) is a transaminase enzyme found in plasma and in various body tissues especially the liver's hepatocytes. Serum ALT is commonly measured clinically as part of a diagnostic evaluation of hepatocellular injury, to determine liver health

# Aladote<sup>®</sup> demonstrates consistent results of reduced liver injury as measured by exploratory biomarkers

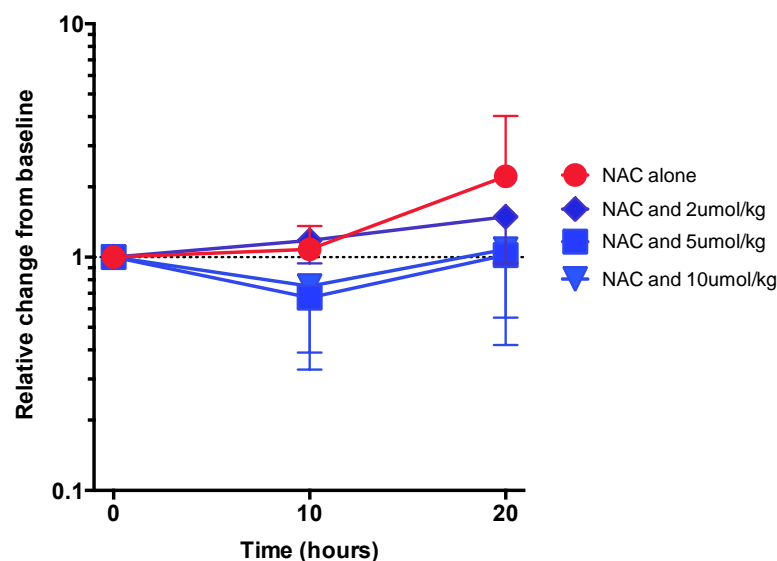


## K18



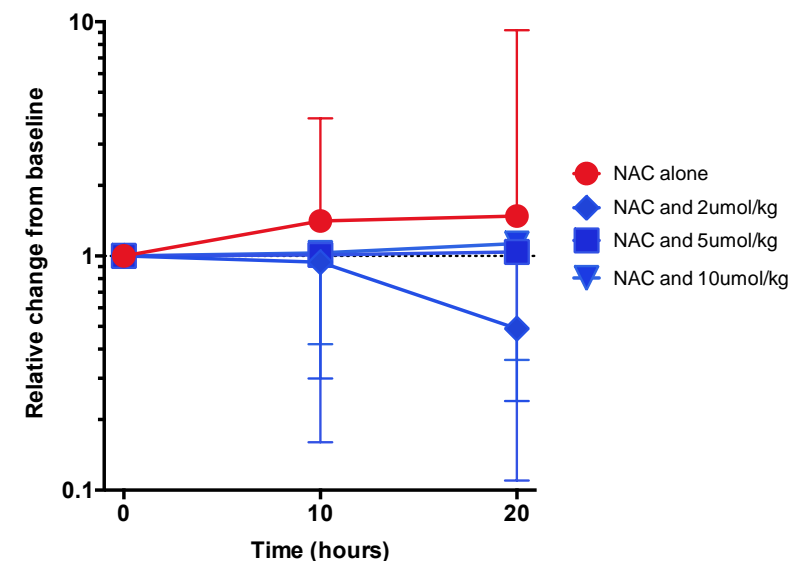
K18 is a measure of cell death and correlate with peak ALT activity during the hospital stay

## ccK18

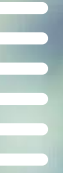


ccK18, is a measure of cell death and correlate with peak ALT activity during the hospital stay

## 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<sup>®</sup> - Regulatory pathway to submissions in EU and US*

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



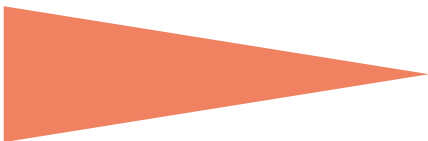
Patient population	<ul style="list-style-type: none"><li>• Patients who have overdosed on paracetamol with increased risk of liver damage due to late arrival at hospital (&gt; 8h) who need treatment with NAC</li></ul>
NAC regimen	<ul style="list-style-type: none"><li>• Approved 21 hours NAC regimen</li></ul>
Treatment groups	<ul style="list-style-type: none"><li>• 4 groups in combination with NAC: <i>Aladote</i> high dose; <i>Aladote</i> middle dose; <i>Aladote</i> low dose; Placebo</li></ul>
Initiation of active treatment	<ul style="list-style-type: none"><li>• IV (bolus) as soon as possible after randomization and after starting NAC treatment (but no later than 4 hours after starting NAC treatment)</li></ul>
Interim analysis	<ul style="list-style-type: none"><li>• Interim analysis after 35 patients per treatment group, which includes a futility analysis, dose selection and analysis of continued study size (number of patients)</li></ul>
Study size	<ul style="list-style-type: none"><li>• 250 patients planned</li></ul>
Efficacy endpoints	<ul style="list-style-type: none"><li>• Primary: Combination of ALT and INR</li><li>• Number (%) of patients who need extended NAC treatment after 21 hours</li><li>• Length of hospital stay</li><li>• Explorative biomarkers: K18, miR-122 and GLDH</li></ul>
Study countries	<ul style="list-style-type: none"><li>• EU, UK and USA</li></ul>



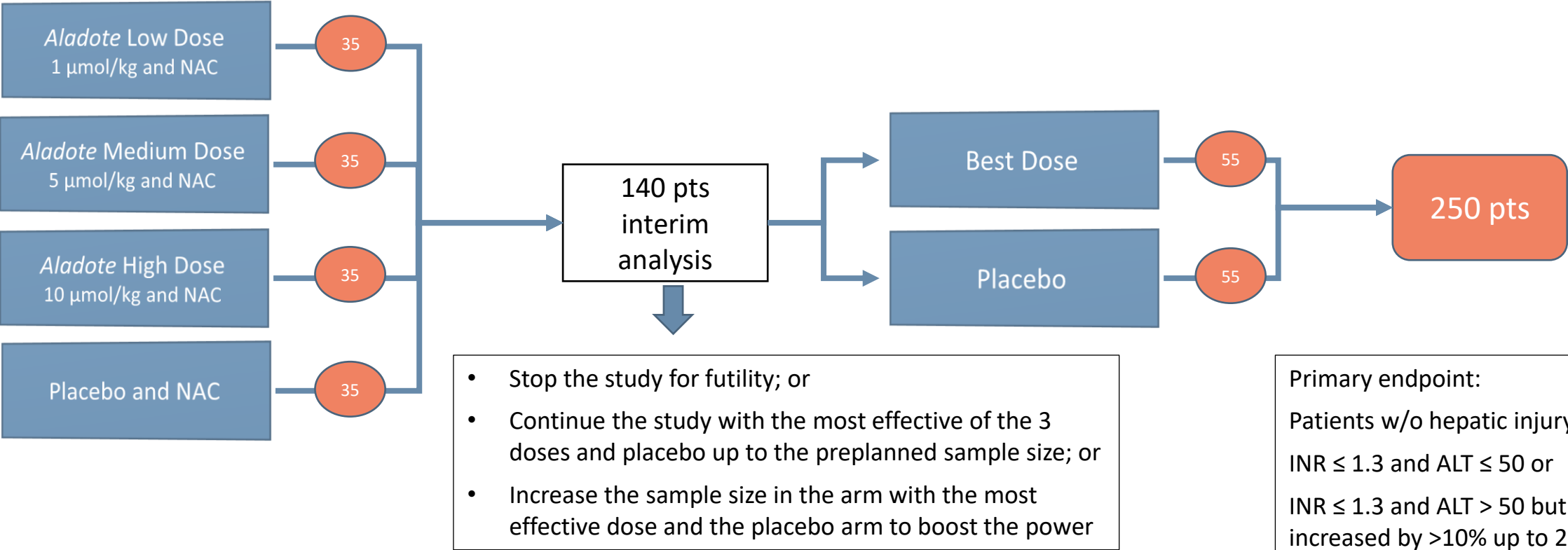
# ALBATROSS: Aladote Phase IIb/III study design



## 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:



# Aladote clinical development timelines



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

2022

2023

2024

2025/26

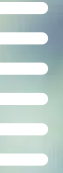
- Start pivotal Phase IIb/III study

- Interim analysis
- Recruitment completed and topline results

- 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<sup>1</sup>
- The POD Emergency Department and inpatient cost is approximately USD 13-40k<sup>1</sup>
- The average POD inpatient length of stay is 3.1 days with a variance of +4.4 days for the most severe cases<sup>1</sup>
- US liver transplant costs USD 125-473k<sup>1</sup>



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**

# 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

- Analogue 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

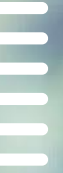
\*Annual number of POD (paracetamol/acetaminophen overdose) cases hospitalized and receiving i.v. antidote (NAC currently the only option), 25% late arrivals (>8h)

# 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

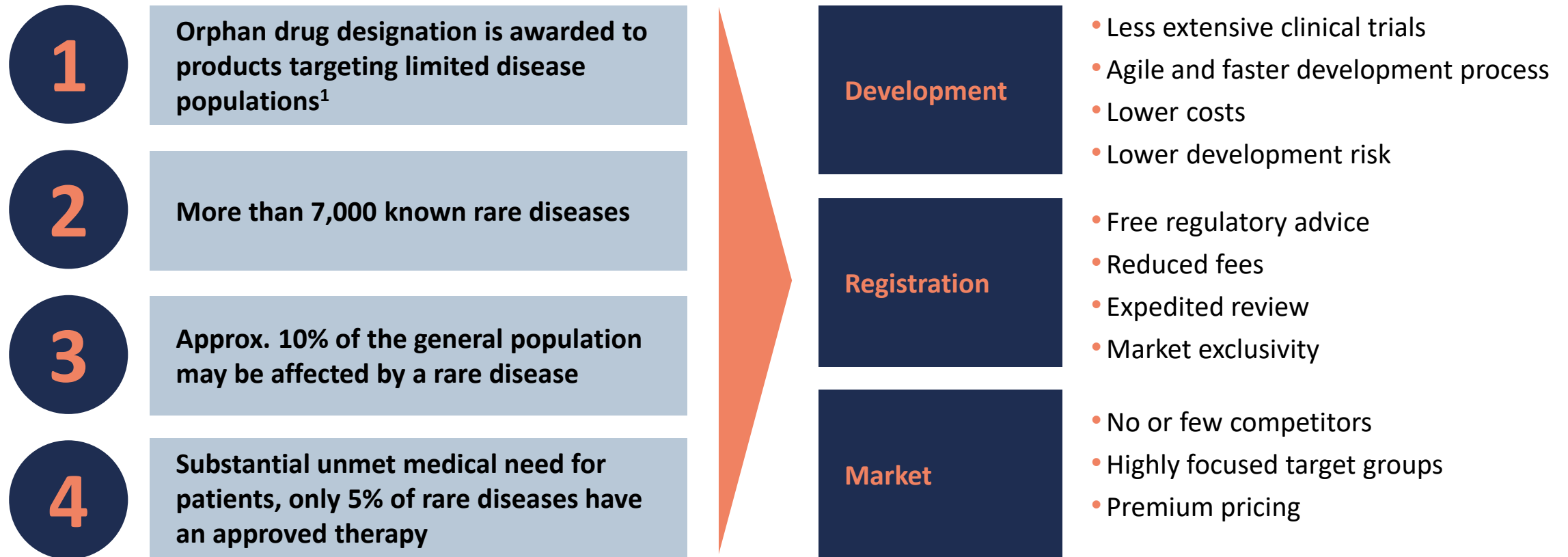
	Naloxone hydrochloride	Praxbind	Andexxa/Ondexxya	Aladote (target profile)
Year of first approval	1971	2015	2018	NA
Poisoning indication	Opioid toxicity	Reversal of anticoagulant effects of the NOAC dabigatran	Reversal of anticoagulant effects of the factor Xa inhibitors apixaban & rivaroxaban	Paracetamol/acetaminophen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



## 4.

### *The attractiveness of the orphan drug segment*

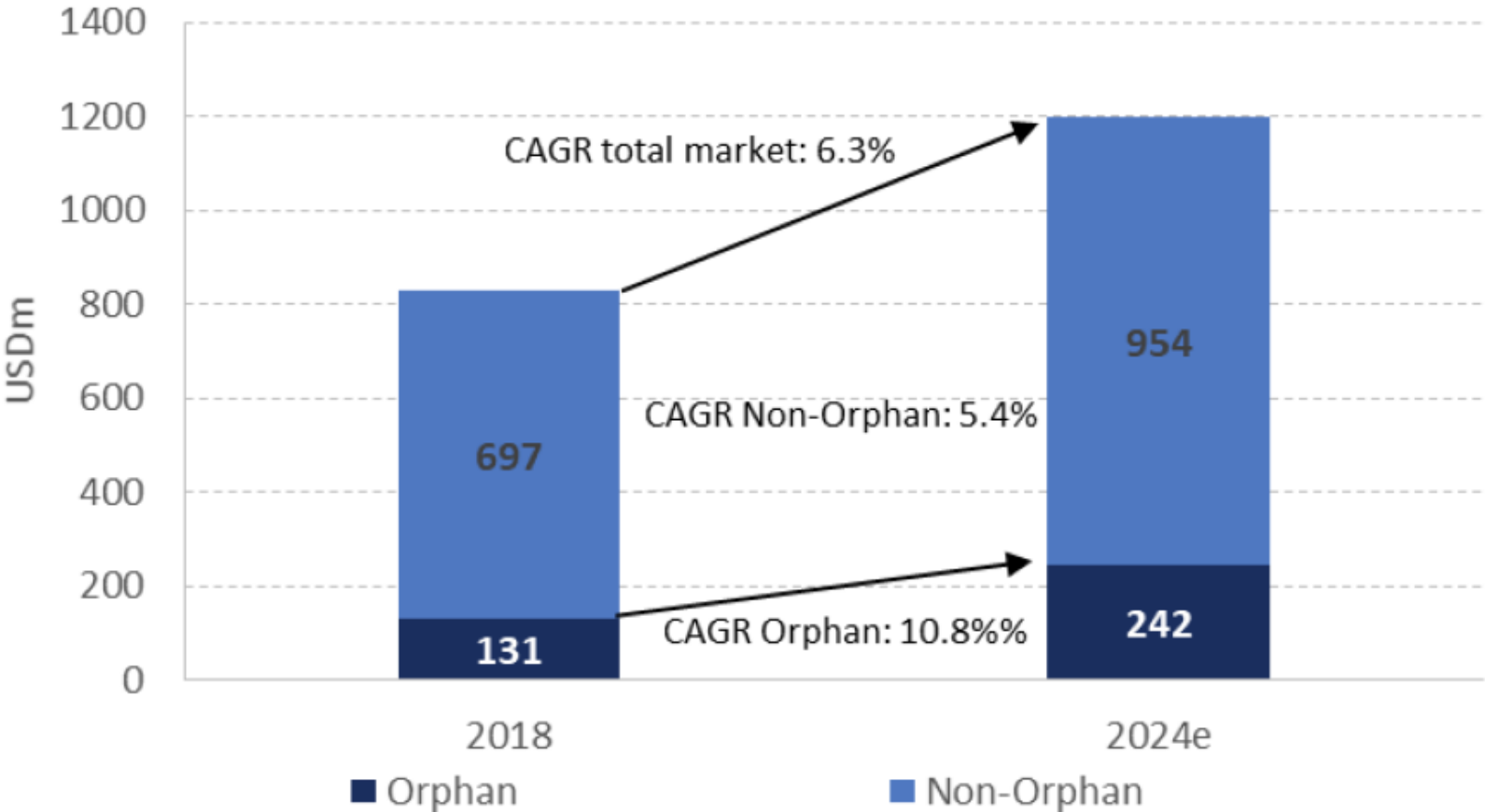
# Orphan drug segment – a highly attractive opportunity

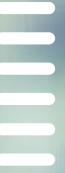


**Well-defined patient populations with substantial unmet medical need**

# 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.*





# 5.

## *Summary*

# EGTX – a de-risked biotech with substantial unlocked potential



- Late stage biotech “under the radar”, developing the first therapy for a devastating genetic disorder
  - Strong team with established track record in the orphan drug space, including SOBI, Alexion, Biomarin, Biogen, Vertex, Sarepta, Shire and Wilson Therapeutics
- Strong and consistent data in clinical trials, demonstrating significant effects on key clinical outcomes
  - Supported by strong mechanistical rationale and data from animal models
- High likelihood to reach market in 2024, already passed most of typical drug development risks
  - All clinical data necessary for regulatory approval in EU already at hand – Submission early autumn 2023
  - A small and short trial reconfirming the effect on biomarker T3 under way to complete the US dossier - Submission Q4 2023
- Significant market opportunity with potential for premium orphan drug pricing
  - Estimated 2,400 affected patients in US and 5,400 in Europe
- Eligible for priority review voucher upon US approval, which can be sold for ~100 MUSD

# Two highly promising orphan drug candidates

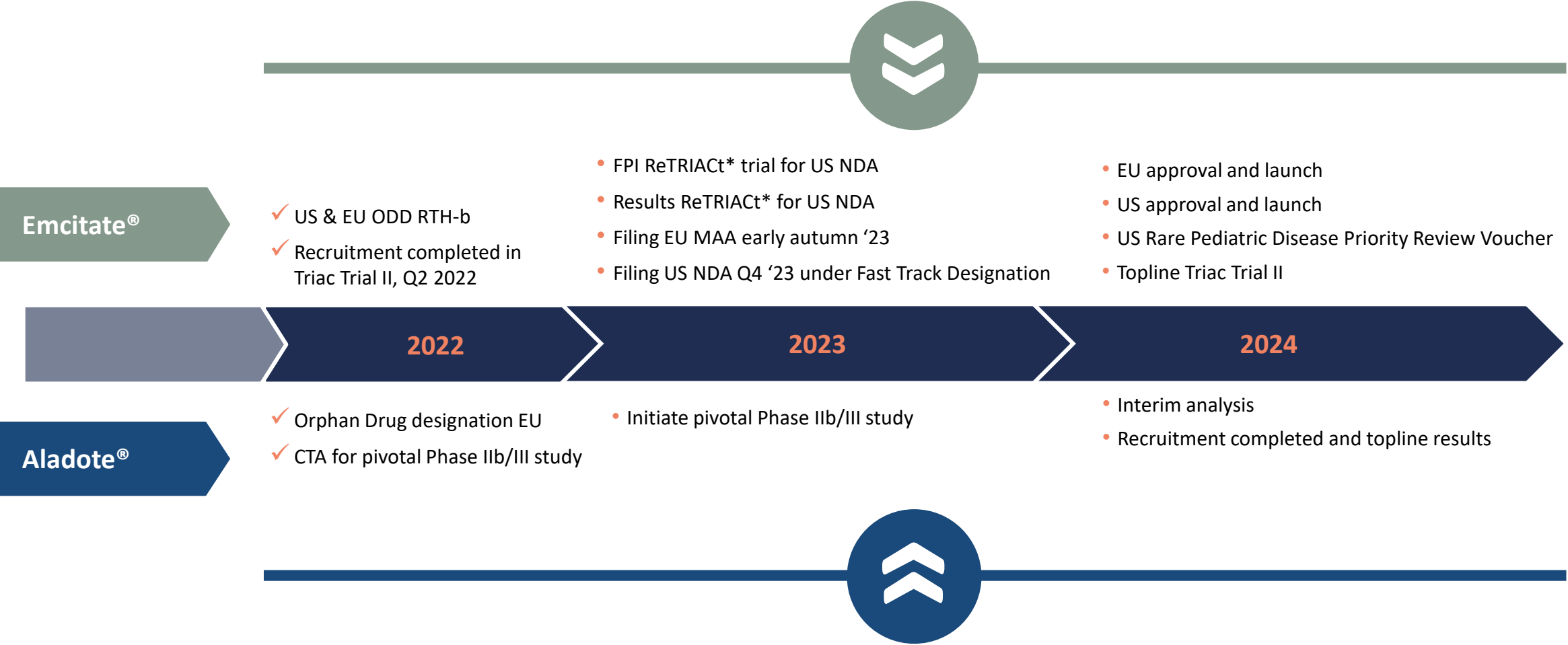
## Emcitate® – Therapy for MCT8 deficiency

- MCT8 deficiency affects ~1:70,000 males: high unmet medical need, no available treatment. No competing sponsored products in clinical development
- Orphan Drug Designation in EU & US
- **US Rare Pediatric Disease Designation**, eligible for Priority Review Voucher. Fast track designation granted by FDA
- Triac Trial I (Phase IIb) completed with **significant** and **clinically** relevant effects on **T3 levels** and **chronic thyrotoxicosis**
- Real-world data published **2021 confirms long-term efficacy and safety** of Emcitate
- **MAA in early autumn 2023**, based on existing clinical data
- **NDA in Q4 2023**, after conducting a 30 days placebo-controlled study in 16 patients to verify the results on T3
- **Triac Trial II fully recruited**; to establish the effects of early intervention on **neurocognitive** development, previously seen in Triac Trial I. Results expected in mid 2024
- Around **180 patients** are being **treated** with Emcitate on a **named patient basis**

## 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, targeting study start in 2023
- No competing products in clinical development

# Upcoming pipeline milestones



\* 16 pts randomized 30 day study for US NDA

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



1

Dedicated orphan drug company  
Two late-stage assets: ***Emcitate*** and ***Aladote***

2

Target **MAA/NDA** submissions:  
***Emcitate 2023*** and ***Aladote 2025***

3

Highly attractive **orphan drug segment** with potential  
**>\$1Bn annual sales opportunity**

4

Plan to **launch** through small **in-house commercial**  
organization in the EU and North America

5

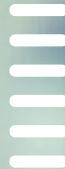
**Strong team** with late-stage orphan clinical development,  
registration and commercialization experience from:

Listed on NASDAQ Stockholm (EGTX)

HQ in Stockholm, Sweden

~30 FTEs





A.

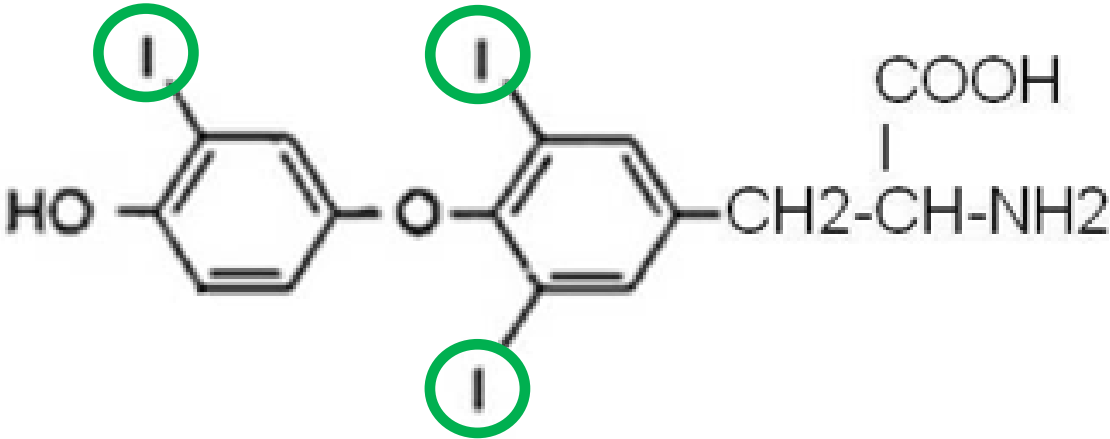
*Appendix*

# Discovery of *Emcitate* (Triac, tiratricol)

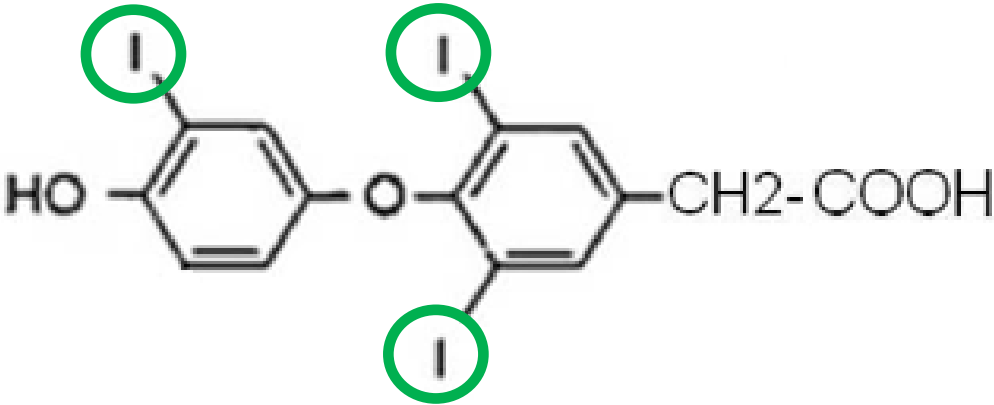


ROSALIND PITT-RIVERS  
M.Sc., Ph.D. Lond.

T3



Triac  
(tiratricol)



## Preliminary Communication

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

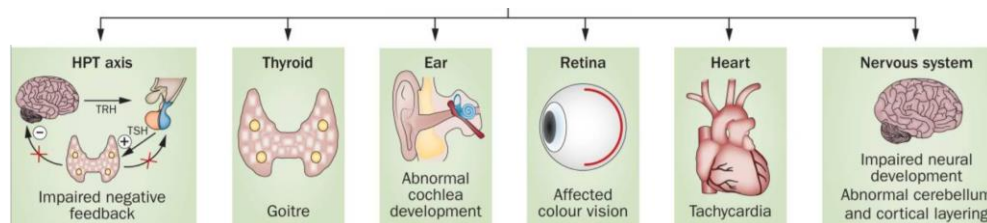
# Resistance to Thyroid Hormone type Beta (RTH-β)

*Potential indication expansion for Emcitate into non-overlapping patient population*

## Characteristics of RTH-β

- Caused by mutations in thyroid hormone receptor beta (TRβ)<sup>1</sup>
- 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<sup>2</sup>
- 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

# 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



**Yilmaz Mahshid, PhD**  
*CFO*

- Joined 2021
- Investment Manager & Controller at Industrifonden
- Sell-side analyst at Pareto & Öhman
- CEO Medivir



**Henrik Krook, PhD**  
*VP Commercial Operations*

- Joined 2020
- Commercial roles at Alexion, Novartis, Roche and Affibody



**Karl Hård, PhD**  
*VP IR, Communications & Business Development*

- Joined 2022
- Redx Pharma, Kiadis, AstraZeneca



**Anny Bedard**  
*President Egetis North America*

- Joined 2022
- Commercial leadership roles at Shire and Sarepta



**Kristina Sjöblom Nygren, MD**  
*CMO*

- Joined 2020
- CMO and Head of Development at Santhera
- 18 years at SOBI, Wyeth & AstraZeneca
- Worked as physician in several clinical positions



**Christian Sonesson, PhD**  
*VP Product Strategy & Development*

- Joined 2017
- AstraZeneca 13 years
- Late stage development expertise from FORXIGA, MOVANTIK, ONGLYZA, BRILINTA & QTERN



**Katayoun Welin-Berger, PhD**  
*VP Technical Operations*

- Joined 2023
- VP Operations at Calliditas Therapeutics
- Previously at BioGaia and AstraZeneca

# Board of directors



**Thomas Lönngren**

*Chair of the board*

- Board member since 2021
- MSc in social and regulatory pharmacy and a degree in Pharmacy, University of Uppsala.
- Previously Executive Director of the European Medicines Agency
- Board member at Compass Pathways and NDA Group



**Peder Walberg**

*Board member*

- Board member since 2020
- Founder and CEO of Rare Thyroid Therapeutics
- MD and BSc in international economy and business administration, Uppsala University
- Other assignments: Board Member of Immedica
- Previous assignments: Founder and CEO, Medical Need, Head of Business Development and Strategy, Swedish Orphan and SOBI. BoD of Wilson Therapeutics and identified Decuprate for treatment of Wilson disease



**Gunilla Osswald**

*Board member*

- Board member since 2017
- PhD in biopharmacy and pharmacokinetics
- Other assignments: CEO BioArctic AB



**Elisabeth Svanberg**

*Board member*

- Board member since 2017
- MD, PhD, Assoc Professor in surgery
- Other assignments: Chief Development Officer Ixaltis SA. Board member Leo Pharma, Amolyt Pharma, Galapagos and EPICS Therapeutics



**Mats Blom**

*Board member*

- Board member since 2021
- BA, Business Administration & Economics, Lund University; MBA, IESE University of Navarra
- Other assignments: CFO NorthSea Therapeutics, Board member Hansa Biopharma, Auris Medical, Altamira Therapeutics and Pephexia Therapeutics

# Share Register and Market Cap

## 10 largest shareholders

Name	Capital	Votes	Num. of shares	Verified
Cetoros AB (Peder Walberg)	13.53%	13.53%	33 776 221	2023-03-29
Cidro Förvaltning AB (Peter Lindell)	10.32%	10.32%	25 760 000	2023-03-29
Fjärde AP-fonden	8.58%	8.58%	21 404 690	2023-03-29
Avla Holding AB (Kennet Rooth)	7.08%	7.08%	17 668 330	2023-03-29
Flerie Invest AB (Thomas Elderred)	5.32%	5.32%	13 280 571	2023-03-29
Handelsbanken Fonder	4.66%	4.66%	11 635 465	2023-04-30
RegulaPharm AB (Gudrun Hörnqvist)	4.22%	4.22%	10 531 660	2023-03-29
Linc AB (Bengt Julander 65.2%)	3.02%	3.02%	7 532 021	2023-03-29
AXA	2.61%	2.61%	6 524 042	2023-03-31
Avanza Pension	2.08%	2.08%	5 189 888	2023-03-29
<b>Total 10</b>	<b>61.42%</b>	<b>61.42%</b>	<b>153 302 888</b>	
Total number of owners	7,419			2023-05-16
Total number of shares	249,589,128			2023-05-16

- **Cash position:** SEK 243M (~EUR 22M)\*
- **Number of outstanding shares:** 249.6M
- **MCap:** ~SEK 1,4 billion\*\*
- **Listing venue:** Nasdaq Stockholm Main Market

Source: Monitor by Modular Finance. Compiled and processed data from various sources, including Euroclear, Morningstar and the Swedish Financial Supervisory Authority (Finansinspektionen). The verification date may vary for certain shareholders

\* At March 31, 2023 (Q1 2023 report); \*\* May 29, 2023

**Acquisition of Rare Thyroid Therapeutics on 5 November 2020**

# The combination will drive synergies

*PledPharma and Rare Thyroid Therapeutics merged to launch a new company*



## PledPharma

- Team with profound late-stage drug development experience and strong track-record
- Listing on Nasdaq Stockholm provides access to public markets and capital as well as visibility
- Desired prospective partner in project collaborations. Previous major license agreement with Solasia
- Efficient internal organisation and strong corporate governance

## Rare Thyroid Therapeutics

- Team with strong track-record of identifying and developing ODDs and creating shareholder value
- Strong network of external project advisors with specialist knowledge. Collaboration with Erasmus Medical Center in Rotterdam
- Founding team with experience from international launch and commercialisation of orphan drugs

## Synergistic orphan drug focus

- 2020 accelerated PledPharma's strategic review
- Lead asset Aladote® facilitates the new pronounced strategic focus on orphan drug segment
- Emcitate® and RTT's capabilities fit well with the new strategy
- Build critical mass, generate synergies and improve operational effectiveness for projects in the orphan segment
- Size, vicinity and complementary capabilities allow for a fast and smooth integration

# The acquisition and rights issue

*Institutional investor base broadened*



## Acquisition

- ✓ On 5 November 2020, PledPharma acquired all outstanding common shares in Rare Thyroid Therapeutics
- ✓ Consideration consisted of a combination of PledPharma common shares and cash
  - An upfront cash payment of SEK 60m
  - 63.8 million shares representing approx 39% of the total number of outstanding shares in PledPharma post rights issues
  - Owners of Rare Thyroid Therapeutics will receive a royalty of 3% of net sales generated through Emcitate®<sup>1</sup>
  - Owners of Rare Thyroid Therapeutics will also be granted 50% of the net proceeds from a potential sale of US Rare Pediatric Disease Priority Review Voucher related to Emcitate®

## Rights issue

- ✓ Successfully raised SEK 250 million in oversubscribed rights issue (c. SEK 200m) and utilized overallotment option (c. SEK 50m)
  - Subscription price of SEK 5.25 per share corresponding to a 2.5 percent premium to close 2 October 2020
- ✓ Institutional investor base broadened
  - Overallotment Option, allocated to the Fourth Swedish National Pension Fund (“AP4”), NYIP (Nyenburgh Holding BV) and Nordic Cross
  - The proceeds will be used to finance: (i) the development of Emcitate® and Aladote® to market approval in Europe and USA (60%); (ii) initial commercial preparations (20%); (iii) general corporate purposes and financial flexibility (20%)

**Thank you!**

Egetis Therapeutics  
[egetis.com](https://egetis.com)