PledPharma and RTT agree to join forces

Creating a new specialised late-stage orphan drug development company

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Agenda

1. **Creating a new specialised late-stage orphan drug development company**
2. Emcitate® - clinical development programme
3. Aladote® - clinical development programme
4. Commercial opportunity and path to market
5. Summary

A. Appendix

Today's presenters

Nicklas Westerholm

CEO

Selected experience

- *International experience from 20 years within AstraZeneca, from roles such as VP Project and Portfolio CVMD, VP Japan Operations, Investor Relations,*
- *Board member, Spago Nanomedical*

Previous experience

AstraZeneca spago NANOMEDICAL

Peder Walberg

Founder and CEO

Selected experience

- *Founder and CEO, Medical Need*
- *Head of Business Development and Strategy, Swedish Orphan International and SOBI*
- *BoD of Wilson Therapeutics and identified Decuprate for treatment of Wilson disease*

rare THYROID THERAPEUTICS

Previous experience

WILSON THERAPEUTICS sobi Pioneer in Rare Diseases Medical Need NOVARTIS

PiedPharma

Creating a specialised late-stage orphan drug development company

1. Dedicated orphan drug development company with two late-stage orphan drug assets: **Aladote®** and **Emcitate®**
2. Highly attractive **orphan drug segment** with potential **USDbn market opportunities**
3. Clear path to market with plan to **launch in EU and US** through niche marketing organisation **within 3 years**
4. Combined core expertise from PledPharma & Rare Thyroid Therapeutics in **late-stage orphan clinical development, registration and launch**
5. Executive leadership team with experience from: sobi, Medical Need, WILSON THERAPEUTICS, NOVARTIS, AstraZeneca

Note: Under name change to Egetis Therapeutics

PledPharma

PledPharma and Rare Thyroid Therapeutics merge to launch a new company for late-stage orphan drug development

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

PledPharma

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

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 commercialization of orphan drugs

rare THYROID THERAPEUTICS

The combination of unique management expertise and multiple programs will drive synergies

Note: Under name change to Egetis Therapeutics

Key terms, conditions and timeline

Acquisition

- PledPharma to acquire all outstanding common shares in Rare Thyroid Therapeutics
- Total offer consideration consists of a combination of PledPharma common shares and cash

Terms of the acquistion

- Owners of Rare Thyroid Therapeutics will receive a royalty of 3% of net sales generated through Emcitate®[1]
- 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®

Acquisition financing[2]

- An upfront cash payment of SEK 60m
- PledPharma to issue approx 63.8 million shares representing 41% of the total number of outstanding shares in PledPharma post-transaction (incl. the contemplated rights issue of c. SEK 200m)

Rights issue[2]

- A fully underwritten rights issue of c. SEK 200m with an overallotment option of c. SEK 50m
- Subscription price of SEK 5.25 per share corresponding to a 2.5 percent premium to close 2 October 2020
- Pro-rata subscription commitments of c. SEK 64m from: the Fourth National Pension Fund (AP4), Nortal Investments AB (Staffan Persson), Cidro Förvaltning (Peter Lindell) (the company's three largest shareholders) as well as Chairman Håkan Åström and CEO Nicklas Westerholm
- Underwriting commitments of c. SEK 136m from: the Fourth National Pension Fund (AP4), Cidro Förvaltning (Peter Lindell), Chairman Håkan Åström and NYIP (Nyenburgh Holding BV)
- The share issue 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%)

Anticipated timing

- Launch of transaction (SPA signed): 5 October 2020
- EGM approval: 28 October 2020
- Record date: 2 November 2020
- Subscription period: 9-23 November 2020
- Outcome of transaction: 26 November 2020

Note: (1) Royalties of 10% on Emcitate® net sales to Erasmus Medical Centre; (2) Subject to EGM approval 28 October 2020

Orphan drug segment represents 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

Combining two highly promising orphan drug candidates in one company

Emcitate®
Therapy for genetic disturbance in thyroid hormone signalling with life-long severe disability

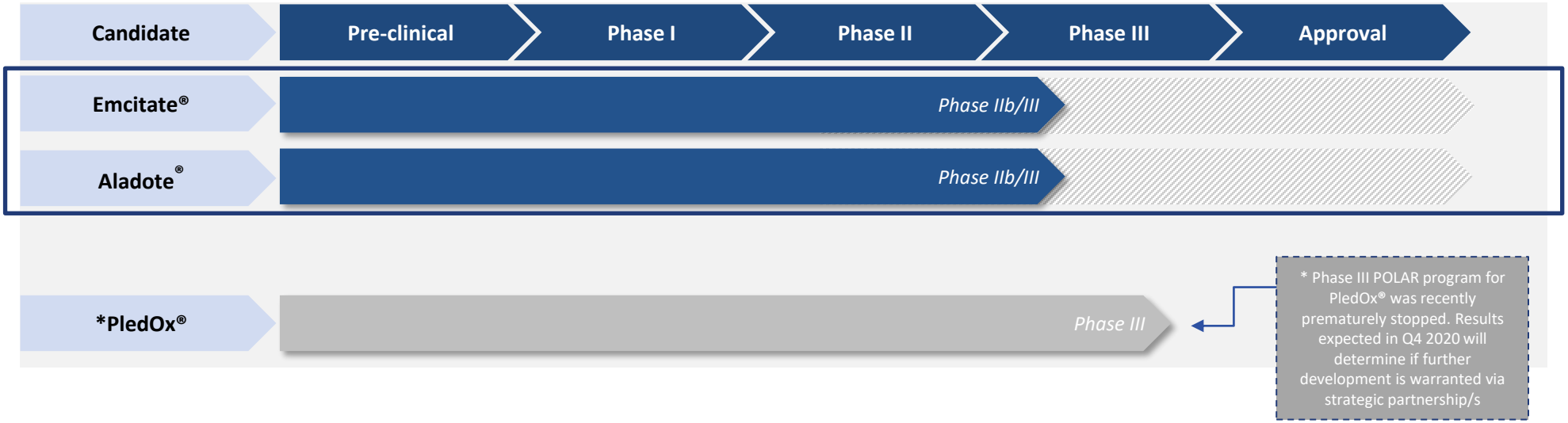
- ✓ Lead candidate for addressing MCT8 deficiency, a condition with high unmet medical need and no available treatment
- ✓ Rare disease which affects 1:70,000 males,
- ✓ Obtained Orphan drug designation in the EU and US 2017 and 2019 respectively. Potentially eligible for Rare Paediatric Disease Designation
- ✓ Phase IIb clinical trial completed with significant and clinically relevant effects
- ✓ Pivotal Phase IIb/III early intervention trial in young subjects planned to start H2 2020
- ✓ No competing products in clinical development

rare THYROID THERAPEUTICS

Aladote®
Prevents acute liver injury caused by paracetamol poisoning

- ✓ Paracetamol poisoning is one of the most common overdose with approx. 135.000 hospital admissions in US/EU5 per annum
- ✓ No adequate treatment for increased risk patients exists
- ✓ Orphan drug designation (ODD) granted in 2019 in the US
- ✓ Eligible for ODD in the EU as a results of Brexit, application under development
- ✓ Successful results from Phase Ib/IIa study in paracetamol overdosed patients
- ✓ Pivotal Phase IIb/III study planned for marketing authorisation application in both US and EU, ongoing interactions with the regulatory agencies (FDA, EMA and MHRA) to finalize study specific details
- ✓ No competing products in clinical development

Late-stage orphan drug pipeline addressing billion dollar markets



Rare Thyroid's candidate Emcitate®

PledPharma's candidate Aladote®

Upcoming pipeline milestones

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Emcitate®

2020	2021	2022	2023	2024
• FPFV pivotal Phase IIb/III early intervention trial	• LPFV pivotal Phase IIb/III early intervention trial	• 12m interim analysis Phase IIb/III early intervention trial	• Filing EU/US	• First EU/US approval and launch

Aladote®

2020	2021	2022	2023	2024
• Regulatory interactions FDA & EMA	• Initiate pivotal Phase II/III study • Orphan Drug designation EU	• Interim analysis	• Filing EU/US	• First EU/US approval and launch

PledOx® Results Phase III POLAR program in Q4 2020

PledPharma

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MCT8 deficiency a detrimental condition with significant unmet medical need

What is MCT8 deficiency?

- **Genetic disorder** resulting in **impaired thyroid hormone trafficking** across cellular membranes
- Mutation located to the X chromosome, **affecting only males**
- Estimated prevalence of **1:70,000** males

What does it mean?

- **Too high and too low thyroid hormone stimulation** in different tissues
- MCT8 deficiency leads to **low or no thyroid hormone levels in the brain**
- Compensatory **increase in circulating thyroid hormone** affects other organs e.g. heart, liver, kidney

What are the challenges?

- Initial symptoms appear within the first months of life, including **muscle hypoplasia**, hypotonia, spasms and seizures with **severe neurocognitive disability**
- Most patients never develop ability to sit or walk and remain **dependant on caregivers** throughout their entire life

How do you manage the disease?

- Currently **no therapy available** to address the underlying thyroid hormone trafficking defect
- Standard therapeutic approaches for thyroid dysfunction not effective
- **Significant unmet medical need** from a humanitarian, health economic and societal perspective

 Source: Groeneweg et al; Lancet D&E 2020, Schwarz et al; Clin Endocrinol & Met 2007

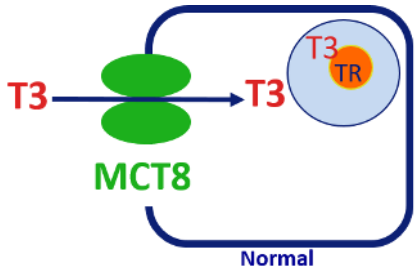
Orphan drug candidate with clear scientific and mechanistic rationale and established safety profile

Difference normal MCT8 and deficiency of MCT8

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

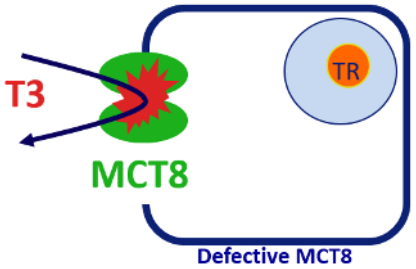
Normal MCT8
- Functional thyroid gland producing T3
- Functioning production of MCT8

➔ T3 cross the cellular membrane and enters the target cell ✓



Mutated MCT8
- Functional thyroid gland producing T3
- MCT8 deficiency leads to absence or loss of function of MCT8 on the cell surface

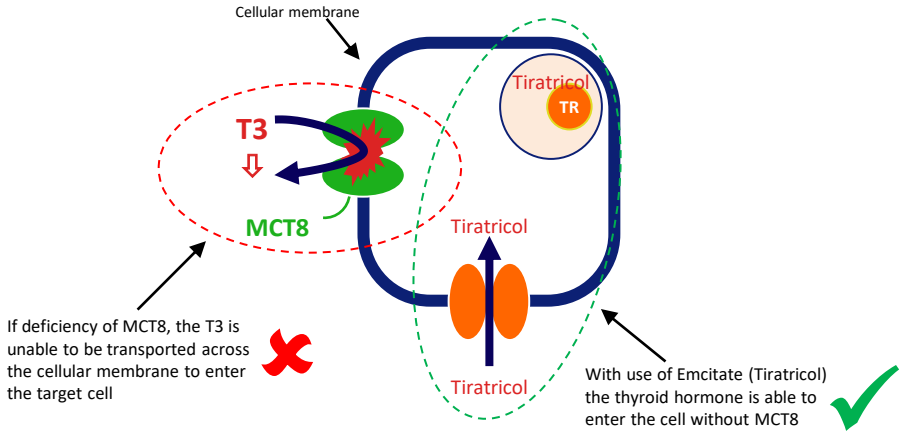
➔ T3 cannot cross the cellular membrane and fails to enter the target cell ✗



Emcitate (tiratricol) – Addressing the MCT8 deficiency

- Tiratricol is a thyroid hormone analogue with high chemical and structural similarity to T3
- 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 company

Emcitate in action



Overview of completed Phase IIb

Primary objective and results

- Evaluate the efficacy and safety of oral administration of tiratricol in male patients with MCT8 deficiency of all ages

Secondary objective and results

- Highly significant primary outcome
- Significant and clinically relevant effects observed across secondary endpoints

Description

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

Endpoints

- Change in T3 serum concentrations
- Change in other thyroid hormone function tests
- Change in thyrotoxic symptoms and markers

# of patients

- 46 MCT8 patients in 9 countries

Encouragement to file product based on data from Phase IIb from EMA SAWP[1)] at protocol assistance meeting in July 2018

Timetable

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

THE LANCET
Public Health

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 Pavone, Klara Rozenkova, Jana Malikova, Adri van der Walt, Irenaeus F M de Coo, Anne McGowan, Geeta Lyons, Femke E Aarsen, Diana Barca, Ingrid M van Beynum, Marieke M van der Knoop, Jurgen Jansen, Martien Manshande*, Roelinneke J Lunsing, Stan Nowak, Carstiaan A den Uil, M Carola Zillikens, Frank E Visser, Paul Vrijmoeth, Marie Claire Y de Wit, Nicole I Wolf, Angelique Zandstra, Goutam Ambegaonkar, Yogen Singh, Yolanda B de Rijke, Marco Medici, Enrico S Bertini, Sylvia Depoortere, Jan Lebl, Marco Cappa, Linda De Meirleir*, Heiko Krude, Dana Craiu, Federica Ziberdi, 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_4 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)30212-7

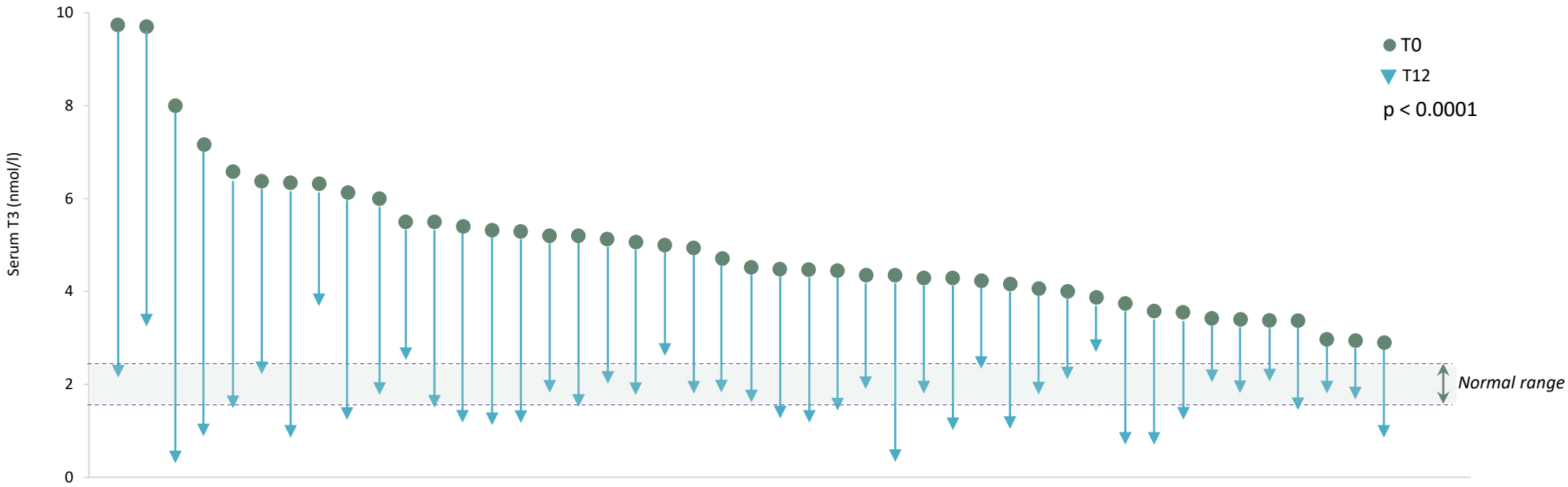
*Dr Meirleir died in August, 2018; Prof De Meirleir died in October, 2018; and Prof T J Visser died in March, 2018.

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 (J F M de Coo MD, F E Aarsen 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

www.thelancet.com/diabetes-endocrinology Published online July 31, 2019 http://dx.doi.org/10.1016/S2213-8587(19)30155-X 1

 Source: Groeneweg et al, Lancet D&E 2019; Note: (1) European Medicines Agency, Scientific Advice Working Party

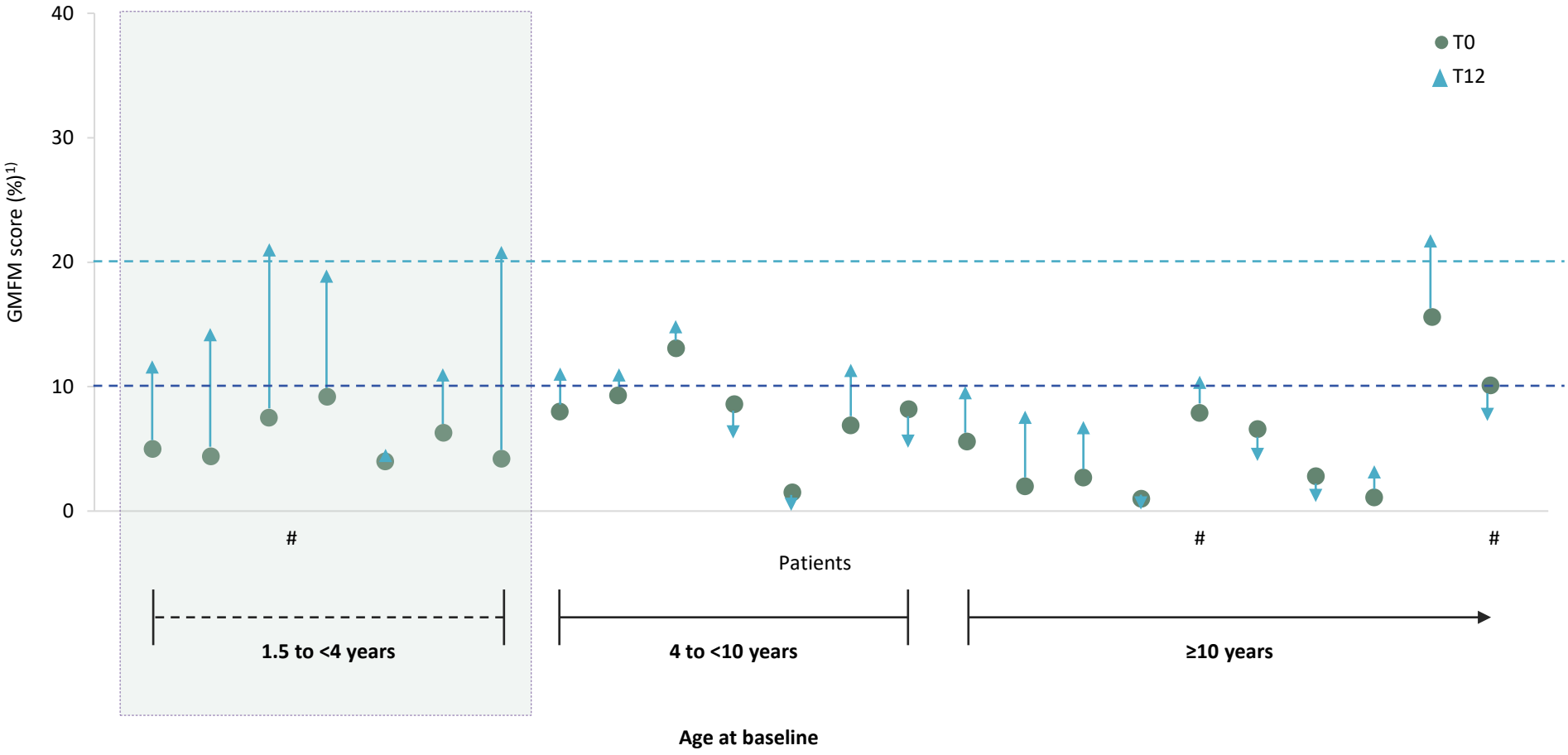
Consistent and highly significant results in completed Phase IIb trial



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 to 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

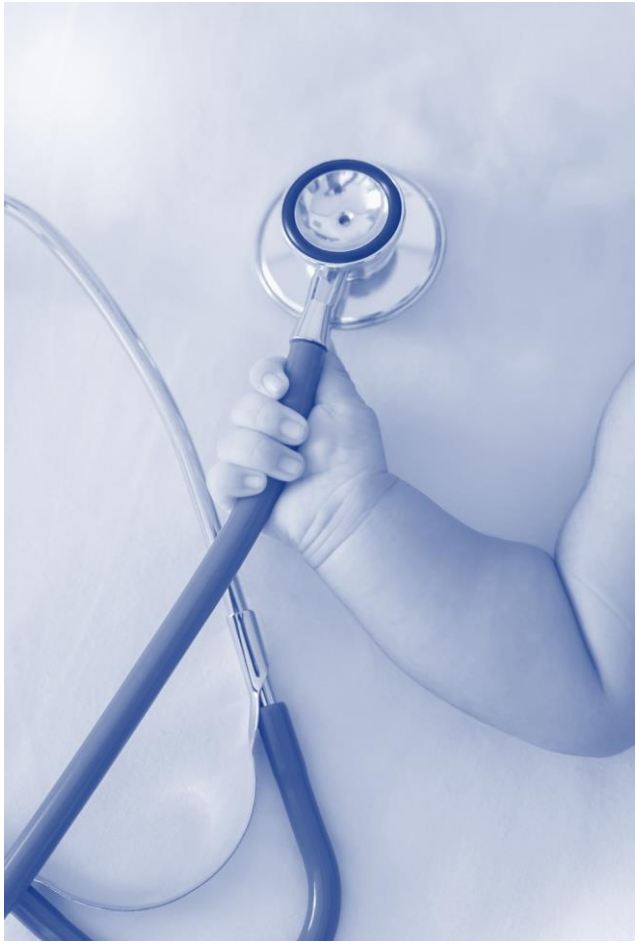
Indication of positive effect on neurocognitive development in the youngest patients



 Source: Groeneweg et al; Lancet D&E 2019

Planned Phase IIb/III early intervention trial design

Primary objective	• Improvement of neurocognitive development
Secondary objective	• Achievement of motor milestones (e.g. hold head, sit independently) • Confirm findings from Triac I Trial in youngest age group
Description	• An open label, multi-centre trial in very young children with MCT8 deficiency • International trial with 10 centres in both Europe and North America • Design discussed and anchored with EMA and FDA
Endpoints	• Improvement in neurocognitive development as measured by GMFM[1)] and BSID-III[2)] compared to natural history controls • Achievement of motor milestones • Normalisation of thyroid hormone function tests and markers of thyrotoxicosis
# of patients	• 15-18 children 0-30 months of age
Preliminary timetable	• Regulatory approval in place in all markets: CZ, DE, IT, UK, FR, NL, US • Start pending COVID situation, FPFV[3] presently expected in H2 2020, LPFV[4] in H2 2021 • Results from interim analysis at 12 months expected in H2 2022



 Note: (1) Gross motor function measure; (2) Bayley Scales of Infant Development; (3) First patient first visit; (4) Last patient first visit

Clinical development timeline

2017

- ✓ Licensing of IP, data and know-how within thyroid hormone signalling disorders from Erasmus Medical Centre [1]
- ✓ EU Orphan Drug Designation
- ✓ Elected for funding by EUREKA EUROSTARS

2018

- ✓ Acquisition of all rights and assets relating to Teatrois in France
- ✓ Triac I Trial completed
- ✓ EMA Protocol Assistance

2019

- ✓ US Orphan Drug Designation
- ✓ Publication Triac Trial
- ✓ FDA pre-IND meeting
- ✓ CTA submissions EU

2020

- CTA approvals in EU
- IND submission
- IND open (SMP)
- FPFV[2] pivotal Phase IIb/III early intervention trial

2021

- Completed recruitment (LPFV) Triac Trial II

2022

- Launch preparations
- Filing EU MAA and US NDA
- Interim (12 month) analysis[3]

2023

- EU and US approval, pricing and launch
- Publication of complete study data (24 month)

 Note: (1) Erasmus Medical Centre; (2) First patient first visit; (3) Provided compelling data in 12 month interim analysis of Phase IIb/III early intervention trial

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Paracetamol poisoning – no adequate treatment for increased-risk patients

What is paracetamol poisoning?

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

How many does it affect?

- **19 billion** units of paracetamol packages are sold in the **US alone** every year
- **89,000 cases/year of paracetamol overdose in the US and 105,000 cases/year in the UK**
- ~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

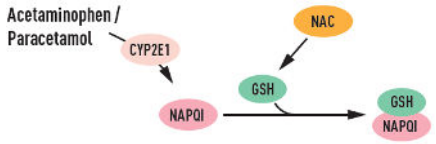
- **Aladote®** aims to become **a new standard of care** for patients with increased risk for liver injury in combination with NAC

Orphan drug candidate with clear scientific and mechanistic rationale

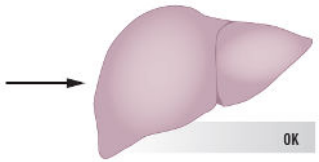
Early presenters (<8h)

NAC treatment effective against liver injury

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



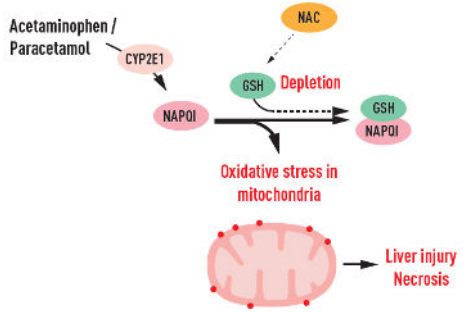
- In most cases NAC effectively prevents liver injury i.e. limited need for Aladote®



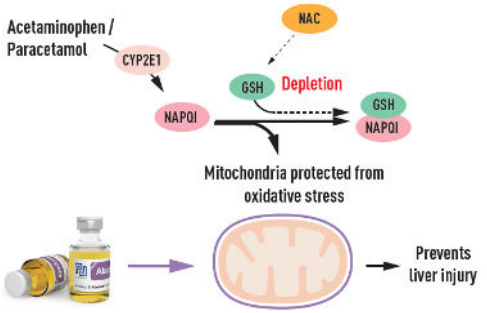
Late presenters (>8h) are at increased-risk for liver injury

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**



 Source: Burke et al. 2010

Overview of completed Phase Ib/IIa

Primary outcome	• Safety and tolerability of Aladote® co-treatment with NAC
Secondary outcomes	• Alanine transaminase (ALT), international normalised ratio (INR), keratin-18, caspase-cleaved keratin-18 (ccK18), microRNA-122 and glutamate dehydrogenase (GLDH)
Description	• An open label, rising-dose, randomized study exploring safety and tolerability of Aladote® co-treatment with NAC • ClinicalTrials.gov identifier: NCT03177395
Endpoints	• Adverse Events and Serious Adverse Events • Secondary endpoints such as ALT and biomarkers of liver damage
# 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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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]

[a] Pharmacology, Therapeutics and Toxicology Unit, Centre for Cardiovascular Science, University of Edinburgh, UK
[b] Edinburgh Clinical Trials Unit, UK
[c] Emergency Medicine Research Group, Royal Infirmary of Edinburgh, UK
[d] PledPharma AB, Stockholm, Sweden

PledPharma

Positive proof-of-principle Phase Ib/IIa results

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%)

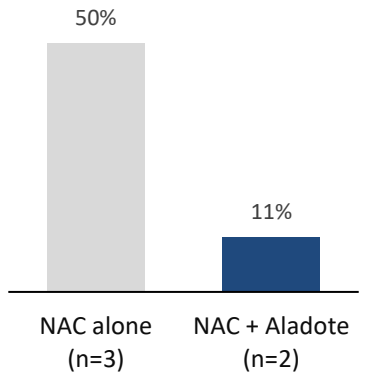
- Met primary endpoint of safety tolerability in the combination of Aladote® and NAC
- **No AE or SAE probably or definitely related to Aladote®**

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

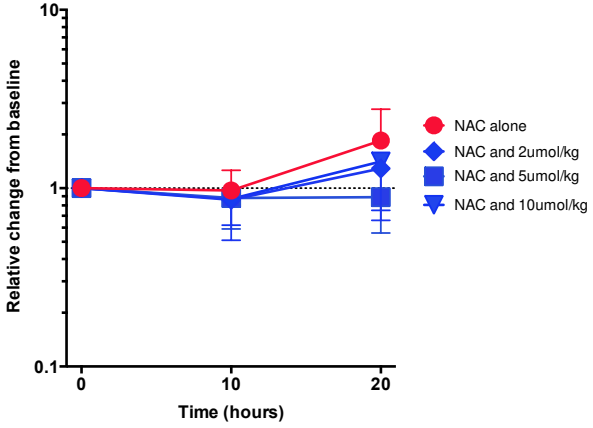
% of patients needing additional NAC infusions after planned 12h NAC infusion



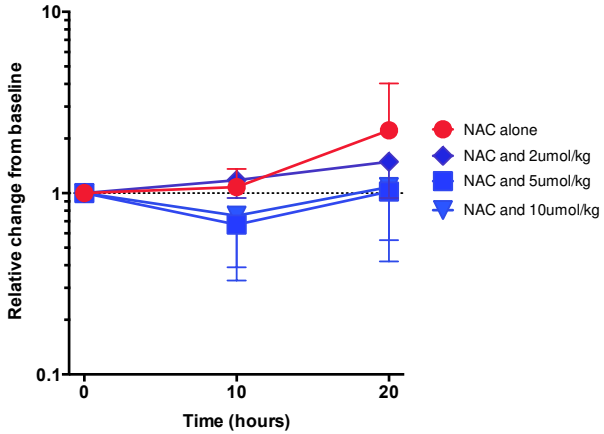
Note: (1) Alanine transaminase (ALT) is a transaminase enzyme also called alanine aminotransferase (ALAT). ALT is found in plasma and in various body tissues especially the liver's hepatocytes. Serum ALT is commonly measured clinically as part of a diagnostic evaluation of hepatocellular injury, to determine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

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

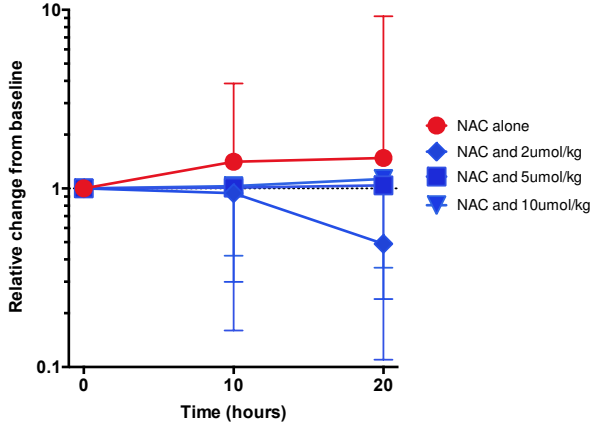
K18



ccK18



miR-122



- K18 and its caspase cleaved form ccK18, is a measure of cell death and correlate with peak ALT activity during the hospital stay
- miR-122 is a liver specific early marker (micro-RNA) for acute liver injury which predicts a rise in ALT activity following paracetamol overdose
- Results of these biomarkers provides scientific support to suggest that **Aladote® may reduce liver injury when added to NAC compared to NAC alone**

Note: miR-122 is a biomarker specific for liver injury and fully conserved (translational) across in vitro models, in vivo models and humans. MiR-122 is an early marker for acute liver injury which predicts a rise in ALT activity following paracetamol overdose. In paracetamol overdose, the full-length variant of K18 is released by necrotic cell death. A shorter, caspase cleaved form of K18 is released following cell apoptosis (programmed cell death). Both forms of K18, measured in the first serum sample at presentation at the hospital after paracetamol overdose, correlate with peak ALT activity during the hospital stay. Full length K18 distinguished patients with and without acute liver injury at an early time where ALT activity was still normal

Pivotal Phase IIb/III study for US/EU regulatory submission[1]

Patient population	• Increased-risk POD patients, Late arrivals (>8h) requiring treatment with NAC
NAC regimes	• Licensed 21 hr NAC regime
Initiation of randomized treatments	• IV (bolus) as soon as possible after randomization and after starting NAC (but no later than 4 hours after starting NAC)
Treatment arms	• 3 arms: Aladote® high-dose; Aladote® low dose; Placebo
Interim analysis	• Interim analysis after 50% of patients, that includes a futility analysis and dose selection where the most effective dose will be continued
Sample size	• 225 patients planned
Efficacy endpoints	• Primary: Composite of ALT and INR • Number (%) of patients that need further NAC after 21h • Length of hospital stay • Experimental biomarkers, K18, miR-122 and GLDH
Study countries	• EU and US

 Note: (1) Tentative study design, pending ongoing regulatory interactions to finalize specific study details

Aladote® clinical development timeline

2018

- ✓ Phase Ib/IIa study fully recruited
- ✓ Initial Phase Ib/IIa results
- ✓ Established Scientific Adviosry Board
- ✓ Full Phase Ib/IIa results
- ✓ Submission of ODD

2019

- ✓ US ODD granted
- ✓ Results presented at Society of Toxicology, EASL ILC and Lancet EBiomedicine
- ✓ Regulatory interactions with FDA and EMA

2020/21

- Regulatory interactions FDA & EMA
- Initiate pivotal Phase II/III study
- Orphan Drug Designation EU

2022/23

- Interim analysis
- Regulatory submissions EU/US

2023/24

- First EU/US approval and launch

2032[1]

 Note: (1) Calmangafodipir composition of matter patent expiresc

Agenda

1. Creating a new specialised late-stage orphan drug development company
2. Emcitate® - clinical development programme
3. Aladote® - clinical development programme
4. **Commercial opportunity and path to market**
5. Summary

A. Appendix

Orphan drugs provide an attractive return on investment

Shorter clinical development time[1]

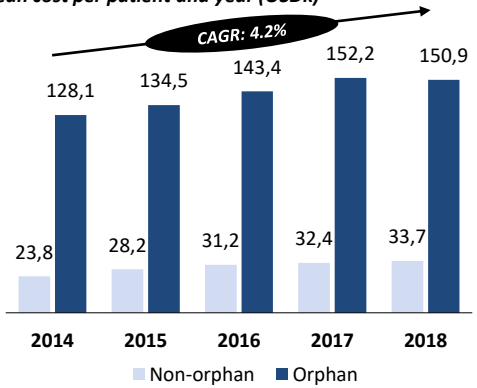
Phase II to launch
Average # of years

ORPHAN — **3.8 years**

NON-ORPHAN — **5.4 years**

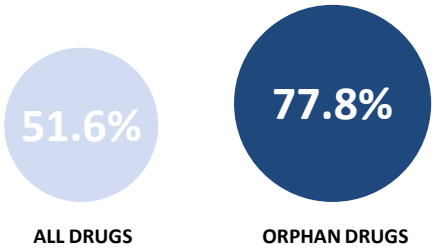
Higher attainable prices[2]

Mean cost per patient and year (USDk)



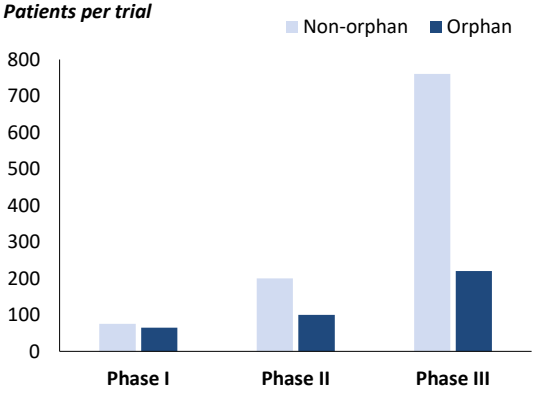
Higher probability of success[3]

Phase III to approval
POS in metabolic/endocrinology indications

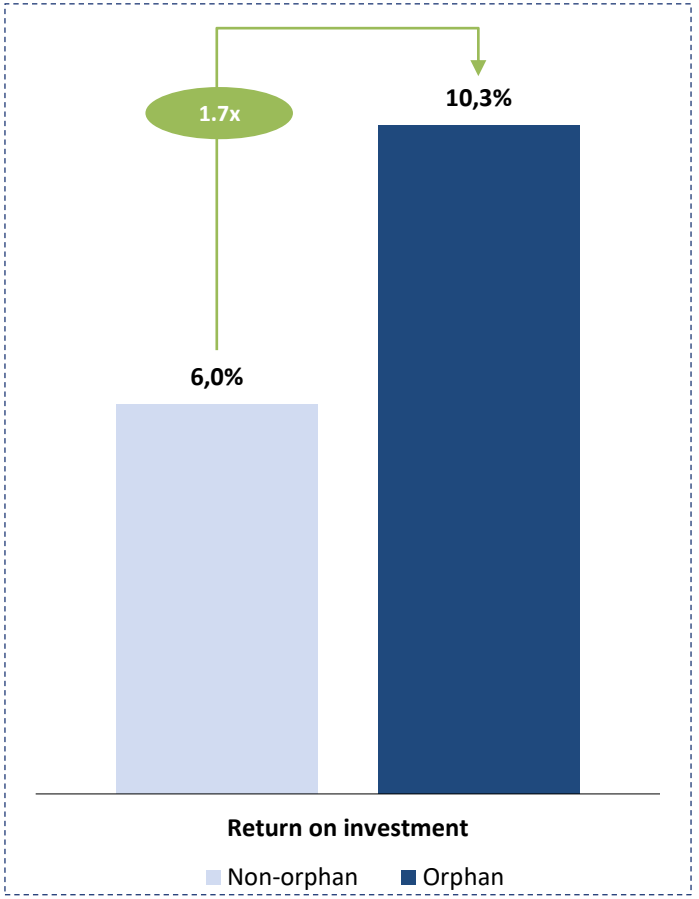


Fewer patients required for clinical trials[4]

Patients per trial



Orphan drugs provide attractive returns[5]



Source: (1) Orphan drugdevelopment: 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

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Emcitate® and Aladote® – alleviating societal burden

Emcitate®

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**[1]

Median life-expectancy of MCT8 patients is **35 years**[2]

Patients underweight for age or without ability to hold head have an even **increased risk of premature death**

Aladote®

In the US the annual cost in 2010 was estimated at **USD 1,059m** to treat patients with POD[3]

The POD Emergency Department and inpatient cost is approximately **USD 13-40k**[3]

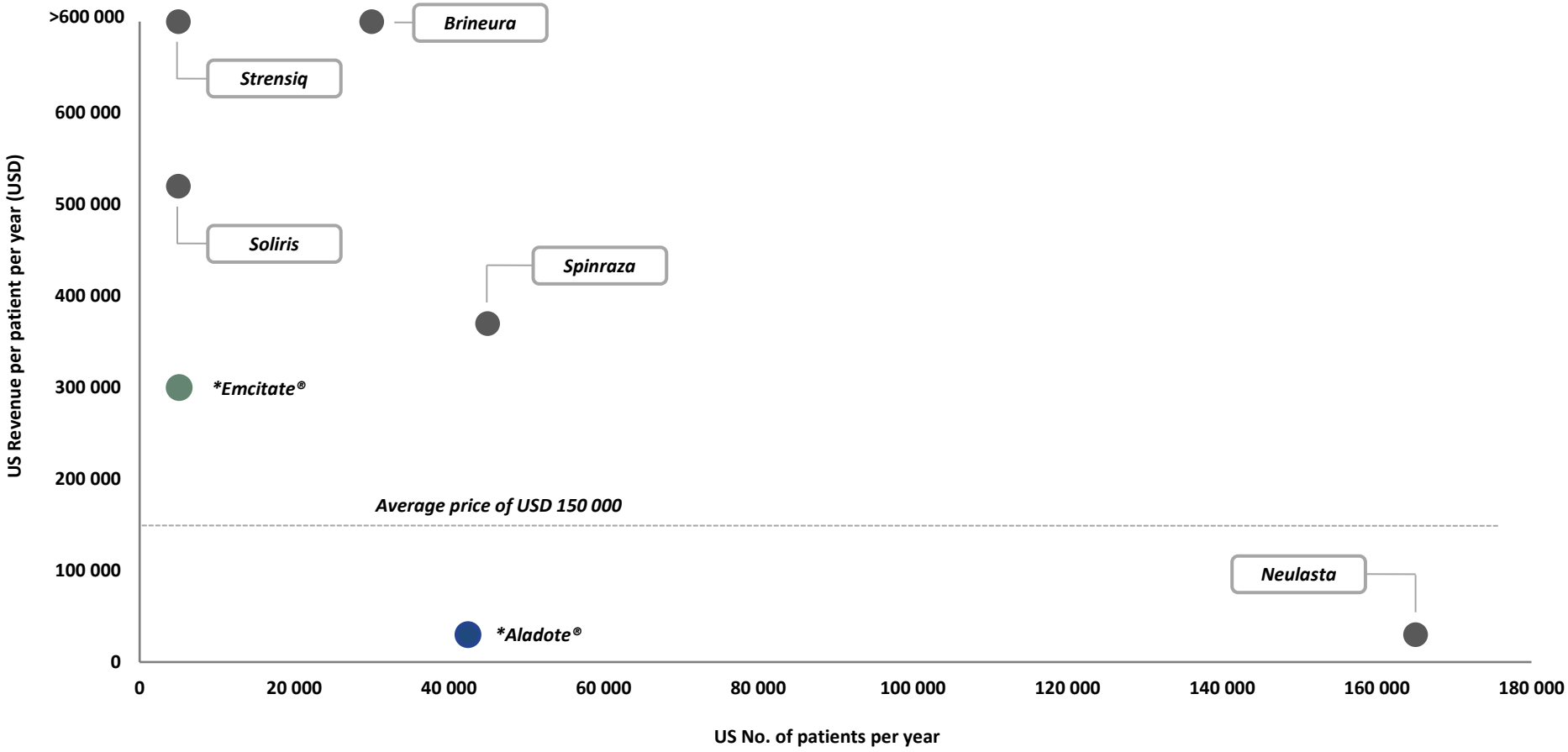
The average POD inpatient length of stay is **3.1 days** with a variance of **+4.4 days** for the most severe cases[3]

US liver transplant costs **USD 125-473k**[3]

Source: (1) Economic burden of spinal muscular atrophy in the United States: a contemporary assessment, Droege et al, Journal of Medical Economics, 2020; (2) Disease characteristics of MCT8 deficiency: an international, retrospective, multicentre cohort study, Groeneweg et al, The Lancet, 2012; (3) Adapted from: Altyar A. Clinical and economic characteristics of emergency department visits due to acetaminophen toxicity in the USA BMJ Open 2015;5;

Orphan drug pricing landscape

2018 US pricing of non-oncology orphan drugs with remaining protection



Note: (*) Expected price points for Emcitate® and Aladote®; Source: EvaluatePharma. FDA Orphan drug designations and approvals database (Downloaded 9 March 2020). Prevalence according to Genetics Home Reference – NIH U.S. National Library of Medicine for underlying conditions for Brineura, Naglazyme and Strensiq.

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Late-stage orphan drug pipeline – a billion USD opportunity

Emcitate®

Target population

10-15,000

1:70.000 males affected[1], 1.5bn people with access to western standard health care[2]

Pricing assumption

200-400,000

USD/per patient per year in the US

COGS assumption[3]

Low single digit percent

Aladote®

Target population

~135,000

Hospital admissions POD patients in US and EU5/year

Pricing assumption

~5,000

USD/dose in the US

COGS assumption[4]

Low single digit percent

Source: (1) 1:50,000-70,000. Visser et al, Clinical Endocrinology 2012; (2) RoW approachable population including Australia, Canada, Japan, Russia, Switzerland, South Korea and Turkey; (3) Based on price assumption of 200,000 USD per patient and year; (4) Based on price assumption of 5,000 USD; Note: Royalties of 10% on Emcitate® net sales to Erasmus Medical Centre

Niche market characteristics enable a small and focused commercial footprint

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

Plan to build **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

Commercialization in other territories through **partners**

Agenda

1. Creating a new specialised late-stage orphan drug development company
2. Emcitate® - clinical development programme
3. Aladote® - clinical development programme
4. Commercial opportunity and path to market
5. **Summary**

A. Appendix

Creating a specialised late-stage orphan drug development company

1. Dedicated orphan drug development company with two late-stage orphan drug assets: **Aladote®** and **Emcitate®**
2. Highly attractive **orphan drug segment** with potential **USDbn market opportunities**
3. Clear path to market with plan to **launch in EU and US** through niche marketing organisation **within 3 years**
4. Combined core expertise from PledPharma & Rare Thyroid Therapeutics in **late-stage orphan clinical development, registration and launch**
5. Executive leadership team with experience from: sobi, Medical Need, WILSON THERAPEUTICS, NOVARTIS, AstraZeneca

 Note: Under name change to Egetis Therapeutics

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Agenda

1 Creating a new specialised late-stage orphan drug development company

2 Emcitate® - clinical development programme

3 Aladote® - clinical development programme

4 Commercial opportunity and path to market

5 Summary

A Appendix

Leadership team

Nicklas Westerholm

CEO

- Took office in June 2017 and has previously worked in the AstraZeneca Group since 1995 in several global roles in various business areas, most recently as VP Project & Portfolio Management. Prior Nicklas has held positions such as Executive Officer & VP Japan Operations, Director Investor Relations, Head of Global API Supply and Head of Development Manufacture. He has studied Analytical and Organic Chemistry at Stockholm University and Chemical Engineering at KTH, as well as studies at University of Warwick, INSEAD and Harvard Business School.
- Ownership: 16,000 shares and 500,000 warrants

Marie-Louise Alamaa

Interim CFO

- Extensive experience within finance and controlling from public companies. Her previous positions include CFO at Index Invest International AB, various senior finance positions at Crucell Sweden AB (previously SBL Vaccin AB) and Senior Consultant at the listed gaming company Stillfront Group AB. She has studied Economics at the Universities of Uppsala and Stockholm, Sweden, with a particular focus on accounting and auditing

Christian Sonesson

VP Product Strategy & Development

- Appointed VP Product Strategy & Development in August 2017 following 13 years at Astra Zeneca. He has broad experience within drug development, including successfully leading products during Phase 3 (FORXIGA® in type 1 diabetes) and of regulatory submissions and defense, bringing new drug candidates to market in different regions (e.g. FORXIGA® in type 2 diabetes, MOVANTIK®, ONGLYZA®-SAVOR, BRILINTA®-PEGASUS and QTERN®). PhD in Biostatistics from Gothenburg University and an Executive MBA from Stockholm School of Economics.
- Ownership: 200,000 warrants

Stefan Carlsson

CMO

- Took office as CMO in November 2017. Med Dr Gothenburg University, where he also has a doctorate in physiology. He has a long experience from leading positions in preclinical and clinical drug development and has published 30 scientific articles in the fields of pharmacology and physiology. Prior to PledPharma , he held positions at AstraZeneca as clinically responsible globally for several products in the market and under development, including Crestor® and Epanova®.
- Ownership: 250,000 warrants

Jacques Näsström

CSO

- Pharmacist with a Ph.D. in Pharmacology from Uppsala University and with an MBA from the Stockholm School of Economics. He has more than 30 years of experience in the pharmaceutical and biotechnology industry, including a position as Investment Manager at Karolinska Investment Fund and various positions in early drug research at Astra and AstraZeneca. CEO of PledPharma between 2010 and June 2017, before that, Jacques worked as research director at Q-Med AB between 2006-2010
- Ownership: 80,452 shares and 20,000 warrants

Scientific advisory board

Established for Aladote®

Dr. Richard C. Dart

- Ph.D., Chair of the Department of Medical Social Sciences at Northwestern University Feinberg School of Medicine in Chicago, USA. Expert in evaluations of patient-reported outcomes in clinical trials.

Professor Laura James

- MD, Associate Vice Chancellor for Clinical and Translational Research and Professor of Pediatrics at the University of Arkansas for Medical Sciences (UAMS) and Arkansas Children's Hospital System, USA.

Peter De Paepe

- MD, Professor in clinical pharmacology at the Heymans Institute of Pharmacology at Ghent University, and is currently head of the emergency department of the Ghent University Hospital in Belgium.

Established for PledOx®

Professor Guido Cavaletti

- MD, Ph.D. and Head of the Neuroimmunology Center at S. Gerardo Hospital and the Experimental Neurology Unit at the School of Medicine, University of Milan-Biocca in Monza, Italy and international expert in chemotherapy induced peripheral neuropathy.

Professor Emeritus Bengt Glimelius

- MD, Ph.D. Professor emeritus in oncology at the University of Uppsala and Consultant at the University hospital. Coordinating principal investigator in the PLIANT trial - PledPharma's Phase IIb Study with PledOx®.

Associate Professor Rolf Karlsten

- MD, Ph.D. Specialist in anesthesiology, intensive care and neuropathic pain management. Head of Rehabilitation Medicine and Pain Center at Uppsala Academic Hospital.

Professor David Cella

- Ph.D., Chair of the Department of Medical Social Sciences at Northwestern University Feinberg School of Medicine in Chicago, USA. Expert in evaluations of patient-reported outcomes in clinical trials.

Fifth undisclosed member

- US expert and KOL In CIPN

Board of directors

Håkan Åström

Chairman of the board

- Board member since: 2011
- Other assignments: Chairman of the boards of directors of Affibody Holding AB, Tubulus RP Förvaltning AB and MedCore AB. Board member of Ferrosan Medical Devices A/S and Rhenman & Partner Asset Management
- Ownership: 505,337 shares and 192,000 warrants

Sten Nilsson

Board member

- Board member since: 2013
- Professor in oncology with affiliation to the Karolinska Institute (KI), MD, Ph.D.
- Other assignments: Board member of the Swedish Cancer Society Research Council and Rhenman & Partner Asset Management
- Ownership: 1,100 shares and 35,000 warrants

Peder Walberg

Incoming Board member*

(*) Appointment subject to EGM approval 28 October 2020

- Founder and CEO of Rare Thyroid Therapeutics
- Other assignments: Board Member of Immedica Pharma AB

Gunilla Osswald

Board member

- Board member since: 2017
- Ph.D. in biopharmacy and pharmacokinetics
- Other assignments: CEO BioArctic AB
- Ownership: 50,000 warrants

Elisabeth Svanberg

Board member

- Board member since: 2017
- MD, Ph.D., Assoc Professor in surgery
- Other assignments: Chief Development Officer Ixaltis SA. Board member Swedish Orphan Biovitrum (SOBI)
- Ownership: 96,000 warrants