PRESS RELEASE
19 June 2024 18:50:00 CEST

Egetis announces topline results of the Phase 2 Triac Trial II with Emcitate® (tiratricol) for MCT8 deficiency

- The numerical improvements versus baseline observed on the primary endpoints of neurocognitive development assessed by the GMFM-88 and BSID-III scales did not show a statistically significant improvement versus historical controls.
- The trial confirmed the significant and durable reduction of endogenous T3 concentrations in all patients and the well-tolerated safety profile of tiratricol seen in previous clinical studies, despite higher dosing per kg body weight compared to previous trials.
- The trial is complementary to the data already submitted and validated in the Marketing Authorisation Application for Emcitate® (tiratricol) for treatment of MCT8 deficiency, based on the benefit of normalization of thyrotoxicosis which has been demonstrated in patients of all ages, as agreed with the European Medicines Agency (EMA). Results from Triac Trial II will be included in the response to EMA 120-day list of questions in August 2024.
- The forthcoming New Drug Application in the USA, will also be based on the already observed treatment effects on T3 concentrations and the manifestations of chronic thyrotoxicosis together with results from the ongoing ReTRIACt trial, as acknowledged by the US Food and Drug Administration (FDA).
- The Company does not consider the approvability of the product to be affected by the Triac Trial II results and the regulatory timelines remain unchanged.
- Conference call for analysts and investors to be held tomorrow Thursday June 20 at 8:00am (CEST).

Stockholm, Sweden, June 19, 2024. Egetis Therapeutics AB (publ) ("**Egetis**" or the "**Company**") (Nasdaq Stockholm: EGTX), today announced that Triac Trial II for the investigational drug Emcitate® (tiratricol) in the treatment of monocarboxylate transporter 8 (MCT8) deficiency, in young patients who were less than 30 months of age at the start of the trial, did not meet its co-primary endpoints. The co-primary endpoints were assessed by changes in the Gross Motor Function Measure (GMFM)-88 total score and the Bayley Scales for Infant and toddler Development (BSID)-III Gross Motor Skill domain, compared to natural history scores from the Triac Trial I. Among key secondary endpoints, total serum thyroid hormone T3 concentrations were reduced significantly and durably in all patients, thereby verifying tiratricol's ability to alleviate thyrotoxicosis in MCT8 deficiency patients.

The trial confirmed the well-tolerated safety profile seen in previous clinical studies, despite higher dosing per kg body weight compared to previous studies.

Professor Dr W. Edward Visser, Principal Investigator of Triac Trial II, Erasmus Medical Center, Rotterdam, The Netherlands, commented: "*Our research hypothesis when we designed the Triac Trial II, based on preclinical data and on exploratory outcomes we observed in Triac Trial I, was to investigate if young patients with MCT8 deficiency might have a neurocognitive benefit from tiratricol treatment, if the treatment is started early. Unfortunately, the study didn't show a clinically relevant and statistically significant improvement on the primary neurocognitive endpoints, but the study confirmed the effects of tiratricol on reducing T3 concentrations, which are relevant to alleviate features of thyrotoxicosis in patients with MCT8 deficiency, regardless of age.*"

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Nicklas Westerholm, CEO of Egetis, commented: *"The safety and tolerability of Emcitate® (tiratricol) is reassuring also when given to young subjects at relatively high doses, although it is disappointing that we didn't meet the primary endpoints in Triac Trial II. The effects on the chronic peripheral thyrotoxicosis already demonstrated in previous studies translate into important clinical benefits to patients of all ages suffering from this devastating condition and we remain confident that tiratricol will become the first approved therapy for MCT8 deficiency and regulatory timelines remain unchanged.*
We are grateful for the patients, their families, and the investigators who have participated in Triac Trial II."

The data will be presented at a forthcoming medical meeting, submitted to a peer-reviewed medical journal and shared with regulatory authorities.

As agreed with the EMA, regulatory approval for Emcitate® (tiratricol) is based on treatment effects on T3 concentration and the manifestations of chronic thyrotoxicosis in MCT8 deficiency, demonstrated in previous clinical studies. This was reflected in the validated marketing authorisation application in the EU, submitted in October 2023. Results from Triac Trial II and will be included in the response to EMA 120-day list of questions in August 2024.

The forthcoming New Drug Application in the USA will also be based on the already observed treatment effects on T3 concentrations and the manifestations of chronic thyrotoxicosis together with results from the ongoing ReTRIACt trial, as acknowledged by the US Food and Drug Administration (FDA).

The timeline for regulatory review and approval in EU remain unchanged. For the US, as previously communicated, the Company will update the market with regards to timelines for NDA submission as soon as 16 evaluable patients have concluded the ongoing ReTRIACt trial.

Webcast and teleconference on July 20 at 08:00am CEST
If you wish to participate via webcast please use the link below. Via the webcast you are able to ask written questions.
https://ir.financialhearings.com/egetis-press-conference-june-2024/register

If you wish to participate via teleconference please register on the link below. After registration you will be provided phone numbers and a conference ID to access the conference. You can ask questions verbally via the teleconference. https://conference.financialhearings.com/teleconference/?id=5007609

About Triac Trial II
Trial II is conducted in patients with MCT8 deficiency, also called Allan-Herndon-Dudley Syndrome (AHDS), which is due to mutations in monocarboxylate transporter 8 (MCT8). MCT8 is a thyroid hormone transporter which is crucial for the transport of thyroid hormone from the blood into different tissues. Defective MCT8 results in a lack of thyroid hormone (hypothyroidism) in tissues that are dependent on MCT8 for thyroid hormone uptake, such as the brain. Hypothyroidism in the brain results in severe intellectual and motor disability. Another important feature of this disease is the high serum T3 concentrations in the blood. This results in thyrotoxicosis in tissues that are not dependent on MCT8 for their thyroid hormone supply. As a result, patients with MCT8 deficiency have clinical features of thyrotoxicosis such as low body weight, elevated heart rate and reduced muscle mass.

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Preclinical studies have shown that the T3 analogue tiratricol is transported into cells in an MCT8-independent manner. In animal models mimicking MCT8 deficiency, tiratricol has been shown to normalize brain development if administrated during early postnatal life.

Triac Trial I (NCT02060474) has shown that tiratricol treatment in patients with MCT8 deficiency improves key clinical and biochemical features caused by the toxic effects of the high T3 concentrations. No drug related serious adverse events occurred during Triac Trial I.

Triac Trial II investigated the effect of treatment with tiratricol in young boys (≤30 months) with MCT8 deficiency. The hypothesis tested is that treatment with tiratricol will have a beneficial effect on the hypothyroid state in the brain as well as the hyperthyroid state in peripheral organs and tissues in these patients. Patients were initially treated for 96 weeks with tiratricol, and the treatment effect was evaluated after 96 weeks. After the 96-week treatment period, patients could enter Part II of the trial, evaluating long-term treatment. Patients will be followed for an additional 2 years, and treatment effect will be evaluated after 3 years and 4 years respectively from start of treatment.

For further information about Triac Trial II, please see https://clinicaltrials.gov/study/NCT02396459

About MCT8 deficiency
MCT8 deficiency, also called Allan-Herndon-Dudley Syndrome, is an ultra-rare genetic disorder. As one of the first X-linked neurodevelopmental syndromes to be described, MCT8 deficiency was later associated with mutations in the *SLC16A2* gene in 2004. The core mechanism driving the pathogenesis of MCT8 deficiency is dysfunction of the thyroid hormone transporter, monocarboxylate transporter 8 (MCT8). MCT8 has a major role in regulating thyroid hormone levels, including the cellular uptake and efflux of tri-iodothyronine (T3) and thyroxine (T4). MCT8 serves an important role in the transport of thyroid hormone across the blood–brain barrier and is also widely expressed in tissues in the thyroid, liver, kidneys, heart, and muscle. This disrupted thyroid hormone homeostasis leads to neurological and endocrinological symptoms. The neurological symptoms are a consequence of too little T3 in the brain during neurodevelopment, whereas the endocrinological symptoms are due to elevated T3 in other organs outside the brain.

Parents of children with MCT8 deficiency usually report the pregnancy and birth as uneventful, and infants appear to develop as expected for the first few months of life. Early signs, such as inadequate head control due to hypotonia and failure to thrive may start to appear from around three months of age, but it usually takes a few more months before medical attention is sought. Recognizing symptoms and making an early diagnosis may help patients and their families.

For further information about MCT8 deficiency, please see www.mct8deficiency.com

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This information is information that Egetis Therapeutics is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact persons set out above, at 2024-06-19 18:50 CEST.

About Egetis Therapeutics

Egetis Therapeutics is an innovative and integrated pharmaceutical company, focusing on projects in late-stage development for commercialization for treatments of serious diseases with significant unmet medical needs in the orphan drug segment.

The Company's lead drug candidate Emcitate® (tiratricol) is under development for the treatment of patients with monocarboxylate transporter 8 (MCT8) deficiency, a highly debilitating rare disease with no available treatment. In previous studies (Triac Trial I and a long-term real-life study) *Emcitate* has shown highly significant and clinically relevant results on serum thyroid hormone T3 levels and secondary clinical endpoints. Egetis submitted a marketing authorisation application (MAA) for *Emcitate* to the European Medicines Agency (EMA) in October 2023.

After a dialogue with the FDA, Egetis is conducting a randomized, placebo-controlled pivotal study in 16 evaluable patients to verify the results on T3 levels seen in previous clinical trials and publications. Egetis will update the market as soon as recruitment has been completed and at that point inform about the timing of availability of top-line results, and the expected timing of the subsequent NDA filing.

Emcitate holds Orphan Drug Designation (ODD) for MCT8 deficiency and resistance to thyroid hormone type beta (RTH-beta) in the US and the EU. MCT8 deficiency and RTH-beta are two distinct indications, with no overlap in patient populations. *Emcitate* has been granted Rare Pediatric Disease Designation (RPDD) which gives Egetis the opportunity to receive a Priority Review Voucher (PRV) in the US, after approval. This voucher can be transferred or sold to another sponsor.

The drug candidate Aladote® (calmangafodipir) is a first in class drug candidate developed to reduce the risk of acute liver injury associated with paracetamol (acetaminophen) overdose. A proof of principle study has been successfully completed. The design of a pivotal Phase IIb/III study (Albatross), with the purpose of applying for market approval in the US and Europe, has been finalized following interactions with the FDA, EMA and MHRA. The study start has been postponed until *Emcitate* marketing authorization submissions for MCT8 deficiency have been completed. *Aladote* has been granted ODD in the US and in the EU.

Egetis Therapeutics (STO: EGTX) is listed on the Nasdaq Stockholm main market. For more information, see www.egetis.com

Attachments

Egetis announces topline results of the Phase 2 Triac Trial II with Emcitate® (tiratricol) for MCT8 deficiency