Press release
9 May 2018
Regulated Information

ThromboGenics Business Update – Q1 2018

Advancing Diabetic Eye Disease Portfolio

Positive Initial Topline Data from Phase 1/ 2a Clinical Study evaluating THR-317, anti-PlGF, for the Treatment of Diabetic Macular Edema (DME)

First patient enrolled in Phase 2 study evaluating anti-PlGF (THR-317) in combination with anti-VEGF (ranibizumab, Lucentis®) in patients with DME

€10 Million equity investment from Novartis Pharma AG

Total cash & investments of €108.5 million as of March 31, 2018

Highlights

Pipeline

- Positive initial results from a Phase 1/2 clinical study evaluating primarily safety, tolerability and biological activity of two dose levels of THR-317 (anti-PlGF) for the treatment of diabetic macular edema (DME) were announced, supporting initiation of a Phase 2 study

- First patient was enrolled in the Phase 2 study evaluating efficacy and safety of intravitreal anti-PlGF (THR-317) administered in combination with anti-VEGF (ranibizumab, Lucentis®), for the treatment of DME

- THR-149 (plasma kallikrein inhibitor) and THR-687 (integrin antagonist) for diabetic retinopathy (DR) and/or DME are on track to enter Phase 1 clinical studies in H1 2018 and mid-2018 respectively

- Further novel diabetic eye disease drug candidates are being studied with at least one expected to enter pre-clinical development in 2018

Financial

- On 26 January 2018, the completion of an equity investment of €10 million by Novartis Pharma AG in ThromboGenics capital was confirmed

- ThromboGenics had, at the end of March 2018, €108.5 million in cash and investments. This compares with €115.7 million as of the end of December 2017. Both figures include €10 million equity investment received from Novartis, as restricted cash in our account on December 31st 2017, and freed up at completion date on January 26th 2018.

Leuven, Belgium – 9 May 2018 – ThromboGenics NV (Euronext Brussels: THR), a biotechnology company developing novel medicines focused on diabetic eye disease, today issues a business update and financial update for the three-month period ending 31 March 2018.

ThromboGenics is developing a broad pipeline of disease modifying drug candidates for the treatment of diabetic eye disease, including:

THR-317 – a PIGF neutralizing monoclonal antibody being developed for the potential treatment of DME. THR-317 is in a Phase 2 study evaluating the efficacy and safety of intravitreal THR-317 administered in combination with Lucentis® (ranibizumab), for the treatment of DME.

THR-149 – a plasma kallikrein inhibitor being developed to treat DME. THR-149 will be evaluated in a Phase 1 open-label, multicenter, dose escalation study evaluating its safety in the treatment of DME, expected to initiate in H1 2018.

THR-687 – a small molecule integrin antagonist being developed to treat a broad range of patients with diabetic eye disease. THR-687 is expected to enter the clinic around mid-2018.

These products all have different modes of action and could allow the Company to address the key segments of the rapidly growing diabetic eye disease market.

Further drug candidates are currently being explored for the treatment of diabetic eye disease and it is expected that at least one additional pre-clinical candidate will be moved into development in 2018.

Patrik De Haes, MD, ThromboGenics CEO, said*: "We have had a busy start to 2018, announcing encouraging Phase 1/2a results with THR-317 and the start of a Phase 2 evaluating THR-317 in combination with Lucentis® in patients with DME. We are also about to progress our plasma-kallikrein inhibitor (THR-149) into the clinic and are on track to start clinical development of our integrin antagonist (THR-687) around mid-2018. We look forward to progressing our diabetic eye disease candidates in the coming months, in line with our strategy of multiple shots on goal."*

ThromboGenics®
Advancing Science. Enhancing Vision.®

Progressing Pipeline of Novel Medicines Targeting Diabetic Eye Disease: Diabetic Retinopathy and Diabetic Macular Edema

According to the International Diabetes Federation, the number of adults with diabetes worldwide is estimated at over 400 million and is expected to increase to over 640 million by 2040.

Diabetic eye disease is caused by hyperglycemia (high blood glucose levels) associated with diabetes. If left unchecked hyperglycemia causes damage to the capillaries in the back of the eye (retina) and can result in vision loss and subsequently, blindness.

Diabetic retinopathy (DR) is the leading cause of vision loss among working-age adults, affecting over a third of all diabetes sufferers[1]. DR progresses from mild, non-proliferative to more severe or even proliferative stages. Diabetic macular edema (DME) is an accumulation of fluid in the macula which can occur at any stage of diabetic retinopathy (DR).

THR-317 – anti-PlGF antibody for treatment of DME

THR-317 (anti-PlGF) is a recombinant humanized monoclonal antibody directed against the receptor-binding site of human placental growth factor (PlGF) being developed for the treatment of DME.

DME represents an area of unmet medical need; the current standard of care treatment with anti-VEGFs has been shown in some cases to result in suboptimal responses in patients.

In March, ThromboGenics **announced initial data from a Phase 1/ 2 study** evaluating safety and efficacy of 2 dose levels (4mg and 8mg) of THR-317 for the treatment of DME.

THR-317 was found to be safe and well tolerated. No dose-limiting toxicities or relevant safety events were reported at either dose level. 30% of the anti-VEGF treatment naïve study subjects treated with THR-317 in the 8mg group showed a ≥15 letter gain from baseline at Day 90 versus 5.3% in the 4mg group.

Final results from this study will be presented at an upcoming ophthalmology conference.

In April, the **first patient was recruited in a Phase 2 study** evaluating the efficacy and safety of intravitreal THR-317 administered in combination with Lucentis® (ranibizumab), for the treatment of DME.

Patients will be randomized into either a combination arm of THR-317 (8mg) + ranibizumab, or ranibizumab plus a sham administration. The study plans to enrol approximately 70 patients, of which around half will be anti-VEGF treatment naïve and the other half will have had suboptimal response to prior treatment with ranibizumab.

[1] International Diabetes Federation (IDF). (2017). IDF Atlas 2017. p.88

The rationale for this study is that combined anti-VEGF (Lucentis®) and anti-PlGF (THR-317) may have a better efficacy than either treatment alone. Non-clinical experiments have shown that addition of an anti-PlGF to an anti-VEGF antibody enhances the inhibitory activity on the growth of new blood vessels (Van de Veire et al., 2010), a disease hallmark of DME.

This means that a combined approach may produce better treatment outcomes. The anti-PIGF component may also target inflammation, another hallmark associated with DME (van Bergen et al., 2017).

Initial results from this clinical study are anticipated by Q3 2019.

THR-149 – a plasma kallikrein inhibitor for treatment of DME

THR-149 is a plasma kallikrein inhibitor being developed to treat DME.

Plasma kallikrein for the treatment of DME acts through inhibition of the Plasma Kallikrein-Kinin (PKaI-kinin) System. Activation of the PKal-kinin system induces retinal vascular permeability, inflammation and angiogenesis. Based on literature data, patients with DME have elevated levels of plasma kallikrein, and the vitreous level of plasma kallikrein varies less compared to VEGF in these patients. Therefore, a plasma kallikrein inhibitor may be appropriate for the treatment of DME patients.

Preclinical studies on bicyclic peptide inhibitors of PKal, such as THR-149, including those published in The Journal of Medicinal Chemistry in March, have demonstrated nanomolar to picomolar potencies, stability in biological matrices and reported prolonged retention in the eye together with *in vivo* efficacy in diabetic models of retinal vascular permeability. These outcomes support THR-149's development as a possible treatment for DME and DR via a VEGF-independent mechanism.

The Company is on track to enrol the first patient in a Phase 1 clinical study evaluating the safety of THR-149 in DME patients in Q2 2018.

THR-687 – an integrin antagonist for diabetic retinopathy, with or without DME

ThromboGenics is developing THR-687, an integrin antagonist, for the treatment of a broad range of patients with DR, with or without DME. THR-687 is expected to enter the clinic mid-2018.

Preclinical studies have provided evidence that THR-687 is a potent and safe treatment, highlighting its ability to inhibit various significant stages in pathologic angiogenesis, an important factor leading to vision loss in diabetic eye disease.

These preclinical data provide support moving into clinical development of THR-687.

Financial review

ThromboGenics had, at the end of March 2018, €108.5 million in cash and investments. This compares with €115.7 million as of the end of December 2017. Both figures include €10 million equity investment received from Novartis, as restricted cash in our account on December 31st 2017, and freed up at completion date on January 26th 2018.

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About ThromboGenics

ThromboGenics is a biopharmaceutical company focused on developing innovative treatments for diabetic eye disease. The company's pipeline of disease modifying drug candidates is targeting the key segments of the diabetic eye disease market.

ThromboGenics' is developing THR-317, a PlGF inhibitor, for the treatment of diabetic macular edema, which is in an ongoing Phase 2 clinical study in combination with ranibizumab (Lucentis®, Novartis). ThromboGenics' late pre-clinical pipeline consists of THR-149, a plasma kallikrein inhibitor, and THR-687, an integrin antagonist. THR-149 is targeted to enter the clinic in H1 2018 and THR-687 around mid-2018. Further new drug candidates are currently being assessed and developed for the treatment of diabetic eye disease.

ThromboGenics owns the global rights to JETREA® (ocriplasmin), the only pharmacological vitreolysis drug approved for the treatment of symptomatic vitreomacular adhesion (in the US) and vitreomacular traction (outside the US).

ThromboGenics is headquartered in Leuven, Belgium, and is listed on the NYSE Euronext Brussels exchange under the symbol THR. More information is available at www.thrombogenics.com

Important information about forward-looking statements

Certain statements in this press release may be considered "forward-looking". Such forward-looking statements are based on current expectations, and, accordingly, entail and are influenced by various risks and uncertainties. The Company therefore cannot provide any assurance that such forward-looking statements will materialize and does not assume an obligation to update or revise any forward-looking statement, whether as a result of new information, future events or any other reason. Additional information concerning risks and uncertainties affecting the business and other factors that could cause actual results to differ materially from any forward-looking statement is contained in the Company's Annual Report.

This press release does not constitute an offer or invitation for the sale or purchase of securities or assets of ThromboGenics in any jurisdiction. No securities of ThromboGenics may be offered or sold within the United States without registration under the U.S. Securities Act of 1933, as amended, or in compliance with an exemption therefrom, and in accordance with any applicable U.S. state securities laws.