ThromboGenics Business Update – Q1 2017

Press release
11 May, 2017

Progressing Innovative Diabetic Eye Disease
Clinical and Pre-Clinical Portfolio

Highlights

• ThromboGenics continues to focus on progressing its portfolio of novel medicines for the treatment of diabetic eye disease

• ThromboGenics recruited the first patients in the Phase II clinical study evaluating THR-317 (anti-PIGF) for Diabetic Macular Edema (DME) in January 2017. The trial is assessing THR-317’s ability to improve best-corrected visual acuity (BCVA) and to reduce central retinal thickness in subjects with DME

• ThromboGenics is conducting a Phase Ila clinical study (CIRCLE) evaluating THR-409 (ocriplasmin) to induce a complete posterior vitreous detachment (total PVD) and prevent patients with non-proliferative diabetic retinopathy from progressing to proliferative diabetic retinopathy, a serious sight threatening condition. Following the CIRCLE study protocol amendment, allowing inclusion of patients with less severe non-proliferative diabetic retinopathy, recruitment has picked up

• ThromboGenics is making good progress with its preclinical pipeline:
  ▪ THR-687 is being developed to treat a broad range of patients with diabetic retinopathy, with or without DME. THR-687 is expected to enter the clinic around the end of 2017
  ▪ THR-149 is being developed to treat edema associated with diabetic retinopathy. ThromboGenics achieved an important milestone in its alliance with Bicycle Therapeutics when THR-149 commenced formal toxicology studies. THR-149 is expected to enter the clinic in H1 2018

• New data presentations and posters (12 in total) delivered at ARVO (the Association for Research in Vision and Ophthalmology), a major ophthalmology conference held in Baltimore, US. The majority of these showed additional positive real world data on ocriplasmin, but also a presentation on ThromboGenics anti-PIGF, THR-317.

• The European Commission confirmed orphan drug designation for TB-403 developed by ThromboGenics’ subsidiary, Oncurious for medulloblastoma, the most common pediatric malignant brain tumor, in January 2017

• Cash and investments were €73.3 million as of the end of March 2017, compared with €80.1 million at the end of December 2016
Leuven, Belgium – 11th May 2017 - ThromboGenics NV (Euronext Brussels: THR), a biotechnology company developing novel treatments for diabetic eye disease, today issues a business update for the three months period ending 31 March 2017.

ThromboGenics is focused on developing novel medicines for diabetic eye disease, particularly diabetic retinopathy (DR) and diabetic macular edema (DME).

Over the last three years, ThromboGenics has developed an attractive pipeline of disease modifying drug candidates. The pipeline consists of THR-409, THR-317, both from its in-house research, as well as THR-149 which resulted from a research collaboration with Bicycle Therapeutics, and THR-687, which was in-licensed from Galapagos NV.

These products all have different modes of action and allow the Company to address the four key segments of the evolving diabetic eye disease market:

- Non-proliferative DR
- Proliferative DR
- Non-proliferative DR with DME
- Proliferative DR with DME

ThromboGenics believes its diabetic eye disease pipeline is one of the strongest in the industry.

Dr. Patrik De Haes, ThromboGenics' CEO, said: “We are making good progress with our exciting drug development pipeline of potential new disease modifying medicines for the treatment of diabetic eye disease. Diabetic Retinopathy and Diabetic Macular Edema (DME) are significant indications where there are clear unmet medical needs and a strong demand for improved or add-on treatment options. With our ambitious pipeline and current cash resources we believe we are well positioned to address all key segments of the diabetic eye disease market and to generate attractive returns for our shareholders.”
Research & Development Activities – Innovative Pipeline Targeting Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)

ThromboGenics pipeline comprises of:

- **THR-317** – a PIGF inhibitor being developed for DME and potentially as a combination therapy for current anti-VEGF treatments. THR-317 entered the clinic at the beginning of 2017. First results are expected in H1 2018
- **THR-409** (ocriplasmin) – is in a Phase IIa (CIRCLE) clinical study evaluating the efficacy and safety of up to 3 intravitreal injections of either 0.125mg or 0.0625mg of THR-409 in inducing total posterior vitreous detachment (PVD) in patients with non-proliferative diabetic retinopathy (NPDR)
- **THR-687** – an integrin antagonist being developed to treat a broad range of patients with DR, with or without DME. THR-687 was in-licensed from Galapagos NV in 2016. THR-687 is expected to enter the clinic around the end of 2017
- **THR-149** – a selective plasma kallikrein inhibitor being developed to treat the edema associated with DR. This compound is the result of the Company’s research collaboration with Bicycle Therapeutics. ThromboGenics will start pivotal toxicology studies before starting the clinical development that is expected in H1 2018

**THR-317 – anti PIGF antibody to treat DME**

ThromboGenics enrolled the first patients in a Phase II, single-masked, multicenter exploratory study evaluating the safety and efficacy of 2 dose levels of THR-317 for the treatment of diabetic macular edema (DME) in January 2017.

THR-317 (anti-PIGF) is a recombinant human monoclonal antibody directed against the receptor-binding site of human placental growth factor (PIGF).

The Phase II study will evaluate the safety of 3 intravitreal injections of 2 dose levels of THR-317 (4 mg or 8 mg). The trial will also assess THR-317’s ability to improve best-corrected visual acuity (BCVA) and to reduce central retinal thickness in subjects with DME.

The study plans to enroll a total of 50 patients (including 10 anti-VEGF treatment resistant patients) over a period of about 12 months. The first results from the study are expected in H1 2018.

ThromboGenics believes that THR-317 could be used as a stand-alone therapy or as an add-on treatment to anti-VEGF medicines, for the treatment of DME or DR.

At the ARVO meeting’s Diabetic Retinopathy session a presentation on THR-317, entitled “Neutralization of placental growth factor as a novel treatment option in diabetic retinopathy”, took place.
THR-409 for Non Proliferative Diabetic Retinopathy – CIRCLE Study

The CIRCLE study is evaluating the ability of multiple doses of THR-409 (ocriplasmin) to induce a total posterior vitreous detachment (PVD) in patients with non-proliferative diabetic retinopathy (NPDR). The study is also assessing the safety of multiple doses of THR-409.

ThromboGenics aims to reduce the risk of disease progression to proliferative diabetic retinopathy (PDR) by inducing a total PVD using THR-409. Research has suggested that total PVD, a complete separation of vitreous and retina, could prevent the progression of NPDR to PDR. The CIRCLE study is a Phase II, randomized, double-masked, sham-controlled, multi-center study that will evaluate the efficacy and safety of up to 3 intravitreal injections of either 0.125mg or 0.0625mg of THR-409 in subjects with moderate to severe NPDR, to induce total PVD in order to reduce the risk of the patient developing sight-threatening PDR.

In December the protocol of the CIRCLE study was amended to allow the trial to recruit from a broader pool of patients. Patient’s recruitment has picked up following this protocol amendment.

The primary endpoint of the CIRCLE study is the percentage of patients with total PVD by the month 3 visit, confirmed by both B-scan ultrasound and SD-OCT.

Furthermore, 2 year follow up of patients may provide insights into THR-409’s potential to reduce the risk of progressing from NPDR to PDR.

Oncurious NV – Developing TB-403 for Pediatric Brain Cancers

Oncurious is developing TB-403 a humanized monoclonal antibody against placental growth factor (PIGF). PIGF is expressed in several types of cancer, including medulloblastoma. High expression of the PIGF receptor neuropilin 1 has been shown to correlate with poor overall survival.

Medulloblastoma is the most common pediatric malignant brain tumor, accounting for 20% of all brain tumors in children. Treatment with TB-403 in relevant animal models for medulloblastoma has demonstrated beneficial effects on tumor growth and survival.

In May 2016, a Phase I/IIa study was initiated with TB-403. The study, which is being conducted by NMTRC, aims to recruit 27 patients with Relapsed or Refractory Medulloblastoma. Patient recruitment is on-going.

The European Commission confirmed the orphan drug designation for TB-403 for medulloblastoma in January 2017. The confirmation by the EC followed an earlier in-depth review and positive opinion on the drug candidate by the EMA Committee for Orphan Medicinal Products (COMP). The orphan designation allows a pharmaceutical company to benefit from incentives from the European Union to develop a medicine for a rare disease, such as reduced fees and protection from competition once the medicine is placed on the market.

BioInvent International is a co-development partner for this clinical program.
**JETREA Update**

**Ocriplasmin Research Findings Presented at ARVO 2017**

New JETREA® research findings were presented at the Association for Research in Vision and Ophthalmology (ARVO) 2017 annual meeting in Baltimore this week.

11 ocriplasmin-related presentations, abstracts and posters were delivered at ARVO. These covered preclinical research findings, real-world clinical data, and further characterization of results from different studies.

A presentation on *ORBIT, a Phase IV Clinical Study – Efficacy and Safety Outcomes* showed the importance of patient selection, with 45.8% of patients seeing VMA/VMT resolution at month 1 post injection. This compares very favorably with the 26.5% resolution rate seen in the MIVI-TRUST Phase III study. The ORBIT study has identified no new safety signals.

The posters and abstracts confirmed the product’s safety profile as described in the approved product label and highlighted the importance of patient selection and the timing of the ocriplasmin injection as crucial for treatment success.

Since its first introduction in early 2013, over 25,000 patients have received a treatment with JETREA®.

**Financial Update**

Cash and investments were €73.3 million as of the end of March 2017, compared with €80.1 million at the end of December 2016.

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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 conducting the CIRCLE study, a Phase II clinical trial evaluating multiple doses of THR-409 (ocriplasmin) to induce a total Posterior Vitreous Detachment in patients with Non-Proliferative Diabetic Retinopathy (NPDR).

Early 2017, ThromboGenics started a Phase II clinical study evaluating THR-317, a PIGF inhibitor for the treatment of diabetic macular edema, as a stand-alone or as a combination therapy with anti-VEGF treatments. In addition, THR-149, a plasma kallikrein inhibitor, which has resulted from research collaboration with Bicycle Therapeutics, and THR-687, an integrin antagonist, which was inlicensed from Galapagos, are in late stage pre-clinical development.

ThromboGenics pioneered a new drug category of pharmacological vitreolysis with JETREA® (ocriplasmin) which is now approved for the treatment of vitreomacular traction in 54 countries worldwide. ThromboGenics is commercializing JETREA® via its subsidiary ThromboGenics, Inc. in the US. Novartis commercializes JETREA® outside the United States.

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.

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