



**Event: ThromboGenics Conference Call**

**Date: 16.03.2017**

**Speakers: Patrik De Haes and Dominique Vanfleteren**

**Call Duration: 20:55**

**Patrik De Haes:** Thank you conference call operator, good afternoon to those listening in Europe and good morning to those in the US. I'm Patrik De Haes, CEO of ThromboGenics, and I would like to welcome you to this conference call covering our 2016 full-year results. On the call with me is Dominique Vanfleteren, our CFO.

I'll begin the call by running through 2016 highlights, and I will then hand over to Dominique who will provide the review of our financial 2016. I then want to focus on providing more detail on the significant market opportunity for novel medicines targeting diabetic eye disease, and the commercial potential of our exciting pipeline of innovative disease-modifying drugs designed to treat diabetic retinopathy. Based on our progress in the last 12 months and our interactions with key opinion leaders, we're optimistic about the potential of this pipeline, which we think is one of the best targeting diabetic eye disease in the industry. I would also like to briefly update you on our oncology spin-off Oncurious, where we are making good progress with the development of TB-403 for paediatric brain cancers. I will then briefly discuss our commercial business based on JETREA, where we have delivered a break-even situation in US in 2016 as promised. I'll then wrap-up before opening the call for any questions you may have.

2016 has being a year where we have refocused our activities and resources on the development of novel disease-modifying treatments for diabetic eye disease. We now have four programmes in development, which together will allow us to target all segments of diabetic retinopathy. We believe we can generate significant value from these markets based on the competitive profiles of our drug candidates. In the last 12 months, we have made good progress with our pipeline; both 409 and 317 are in phase II, while our most advanced pre-clinical candidate, 687, is expected to enter the clinic around year-end. 149 is due to enter the clinic in 2018.

In August 2015, we announced our decision to significantly to reduce the resources that we're allocating to the commercialisation of JETREA in the US for the treatment of sVMA. We implemented this decision in the second half of 2015, and this has enabled our US operations to achieve a cash-neutral situation in 2016.

With this brief introduction, I would like to hand over to Dominique who will run you through our financials.

**Dominique Vanfleteren:** Thank you, Patrik. In 2016, ThromboGenics had total revenues of €7.1 million, including €4.4 million of JETREA sales in the US and €2.5 million in royalties as well as €0.2 million of other income. In the corresponding period in 2015, ThromboGenics reported €7.4 million of JETREA US sales and royalty income of €3.2 million. As Patrik has outlined, a key financial target in 2016 was ensuring that the operations in the US reached a break-even cash-neutral situation, and we are very pleased to have achieved this goal. This was the result of reducing the size of our US organisation in late 2015.

During 2016, we have increased our spending on R&D expenses as we have refocused our efforts on drug development activities. In 2016, our R&D spending was €24.6 million, versus €21.4 million in 2015. This level of spending reflects the cost of the CIRCLE phase II clinical study named THR-149, and the preparations for the start of the phase II trial with THR-317 which commenced in early 2017. We have also been investing in the pre-clinical activities to progress our two THR-687 and THR-149. The other element of our R&D spend was the ongoing Oncurious phase I/II study with the name TB-403.

In line with the reduction in our commercial activities, we have seen a major decrease in sales and marketing expenses. Our overall sales and marketing expenses amounted to €4.3 million in 2016, which compares to €17.6 million in 2015. Just for the reference, we had sales and marketing expenses of €29.9 million in 2014.

In 2016, we reported a net loss of €60.4 million. The reason for this increased loss, despite much improved operating performance, was an impairment charge of €26.6 million related to the carrying value of JETREA in our balance sheet, and due to the anticipated lower sales of JETREA. Excluding this impairment charge, we are looking at a €33.8 million loss for 2016, which compares to €37.9 million net loss we reported in 2015.

Given the break-even situation and our continued tight cash management across the whole ThromboGenics organisation, we ended with cash and cash equivalents of €80.1 million, down from €101.4 million in 2015. And that obviously shows that the impairment had no impact on our cash. With our tight cash discipline, our break-even US organisation and the current levels of cash, as well as some royalties, we now believe that we have the resources to fund our business activities for the foreseeable future. And this time, that will allow us to generate significant value from our four components that comprise our diabetic eye disease pipeline, as well as Oncurious, our oncology spin-off.

With this, I would like now to hand over to you, Patrik.

**Patrik De Haes:** Thank you, Dominique. I would now like to turn why we invest in the development pipeline of novel drug candidates targeting diabetic eye disease. The key reason is that the market for new treatments for diabetic retinopathy is expected to be one of the fastest-growing segments of the ophthalmic medicines market. Over the period to 2023, this market segment is forecast to grow at over 16% per year from €1.6 billion to €4.2 billion, which is more than double the growth rates of the overall ophthalmology market. A key factor underlying this growth is the increasing number of persons with diabetes. At present, there are several hundreds of million people with diabetes worldwide, and this number is expected to double over the next 20 years. Another reason for focusing on this market is that there is a clear need to improve on the treatments for both diabetic retinopathy and diabetic edema that they're currently available.

This growth in the number of people with diabetes is expected to significantly increase the number of patients suffering from diabetic retinopathy. It is estimated that approximately one out of three of all people with diabetes will develop one or the other form of diabetic retinopathy during their lifetime. Diabetic eye disease is a serious disease, and is the leading cause of vision loss in working-age adults.

It is important to recognise that diabetic retinopathy is a progressive disease, with patients experiencing different forms. As you can see, the most common form of the disease is non-proliferative diabetic retinopathy. It's important to treat patients with non-proliferative diabetic retinopathy in order to prevent the condition progressing to the so-called proliferative form, a serious sight-threatening condition. As you can see, a significant number of the DR patients, as they are called, experience also diabetic macular edema, due to leaking of fluid from blood vessels within the macula, and which can progress to cause blindness. Again, there is a clear need for a disease-modifying options to treat this condition.

I would now like to turn to the pipeline of novel disease-modifying drug candidates that we are developing to treat this disease. We have been able to create this pipeline by using our research team's cutting-edge science, which has included the development of a number of proprietary pre-clinical models of DR and diabetic macular edema. As you can see, this pipeline provides us access to all four segments of the diabetic eye disease market.

I will now talk on those four molecules in more detail. 409, or ocriplasmin, is being developed for patients with a non-proliferative form of DR, which is a disease where there is a clear need for disease-modifying treatment options. In December 2016, we announced that we have changed the enrolment criteria for the ongoing phase II clinical study, so-called CIRCLE study, assessing the ability of multiple doses of 409 to induce a complete PVD in patients with non-proliferative DR. The reason for conducting the CIRCLE study is that it's thought that by creating a PVD with 409, we can prevent the non-proliferative form from progressing to the proliferative form, a serious sight-threatening condition. Research has shown that the presence of a PVD – or a posterior vitreous detachment, where the

vitreous is separated from the retina – may prevent the growth of blood vessels that are the cause of DR's proliferative form. This theory is supported by the observation that proliferative DR is rare in patients with a PVD. The changes to the inclusion criteria that we announced in December were designed to give us access to a broader pool of patients and, as a result, speed up the recruitment of the study, and I'm happy to confirm that we're seeing a positive impact of that protocol change.

So, moving to our second candidate, 317, which is being developed for diabetic macular edema, either alone or in combination with anti-VEGF drugs. THR-317 has a novel mode of action, and we are confident that this product, which targets PIGF, will deliver important benefits to DME patients. It is the only drug in development that targets specifically PIGF. It is disease-modifying, and its anti-inflammatory and anti-fibrotic actions are key differentiating factors. We started a phase II trial with THR-317 in January of this year. The design of this study is set out on this slide. As you can see, we intend to recruit patients who have responded poorly to anti-VEGF into this study as well. We're looking forward to seeing what benefit THR can deliver to these patients, and we expect the first results to come in first half of 2018.

I would now briefly update you on our two pre-clinical drugs. The first one where we have made progress in the last 12 months is 687, which is a small molecule integrin antagonist, and we are keen to progress this exciting product as quickly as we can, given that it could potentially be used to treat a broad range of patients with diabetic retinopathy with or without DME.

The next slide gives you a sense of how potent our anti-angiogenic compound, THR-687 is. This is a key property given the important role of new blood vessels' growth in DR. We expect 687 to enter the clinic around the end of the year of 2017.

We're also developing a further compound called THR-149, which is a plasma kallikrein inhibitor to treat edema associated with diabetic retinopathy. We expect the novel drug to have a positive impact on disease onset and progression, and will enter the clinic in 2018.

I will briefly spend a few words on Oncurious, our oncology company in which VIB, a leading life science research institute in Flanders, is our partner. Oncurious is focused on developing orphan drugs for paediatric cancer treatment. The lead product, 403, is a humanised monoclonal antibody against placental growth factor. PIGF is expressed in several types of cancer, including medulloblastoma, and scientific research has shown that PIGF plays a vital role in the brain and that its expression is required for the growth and spread of medulloblastoma. Oncurious is collaborating with the NMTRC, the Neuroblastoma and Medulloblastoma Translational Research Centre, a non-profit US organisation and clinical trial network, to conduct the current ongoing phase I/II trial in patients with medulloblastoma. NMTRC operates a network of 25 clinical centres across the US. BIO event is also contributing to the cost of this study. We would expect to be able to report the first results in the course of 2018. Another positive development for Oncurious over the EC confirmation of the Orphan Drug Designation for TB-403 in Medulloblastoma.

So, I would also like to update you on JETREA for symptomatic vitreomacular adhesion. The key message with regard to JETREA is that we have achieved break-even in the US in 2016 as we were targeted. We now make JETREA available with a much smaller team and a specialised distribution channel. We also continue to provide the retina community with more data on what we still believe is an excellent product for the treatment of sVMA. The OASIS two-year follow-up data showed that JETREA was more effective than the phase III trial result. This outcome was largely due to better patient selection. The efficacy and safety results from OASIS published in *Ophthalmology*, the Journal of the American Academy. I would like to highlight that these data showed that JETREA's safety profile was in line with the product approved label, which is very encouraging. And just to remind you, over 25,000 patients have now been treated with this drug to date. JETREA is now approved in 53 countries outside the US. As you know, Alcon Novartis is commercialising JETREA outside the US.

I will now update you on the news flow which we expect over the coming eight months. As you can see, we expect data read-outs on 409 and 317 in the coming 12 months. In addition, we are expecting to start clinical studies with 687 and 149 in late 2017 and 2018 respectively. We believe these are all milestones which will provide momentum to the ThromboGenics business and highlight the value that we are creating.

In this final slide, I would like to wrap up what we have covered on today's call. As a drug development company, we are now clearly focused on delivering shareholder value through executing a drug development pipeline of innovative treatments, all targeting diabetic eye disease. We are working on novel treatments for DR, both the non-proliferative form and the proliferative form, as well as diabetic macular edema. There are conditions where there is a clear need for improved treatment options.

Our pipeline, which we believe is one of the most exciting in the industry, contains four novel disease-modifying drugs. This pipeline will allow us to target all segments of the fast-growing diabetic retinopathy market. We're confident, based on the clearly differentiated drug candidates, that we will be able to both improve the lives of patients with diabetic eye disease and to generate value for our shareholders. We are in the fortunate position that our current cash resources of €80 million will allow us to finance our clinical development plans for the foreseeable future, and we are confident that within a short timeframe we can deliver a number of potential value-generating milestones.

With that, I would like now to open the call for any questions that you may have.

**Operator:** Thank you. Ladies and gentlemen, if you wish to ask a question please dial 0 and 1 on your telephone keypad. You may also use your webcast platform to submit your questions by writing. Thank you.

We currently have no questions. Ladies and gentlemen, I would like to remind you that if you wish to ask a question, please dial 0 and 1 on your telephone keypad or use the webcast platform. Thank you very much.

We have a first question over the phone from Michaël Vlemmix from KBC Securities. Please go ahead, sir.

**Michaël Vlemmix:** Hi, good evening. Sorry, I had some issues with the dialling. First question: can you give a little bit more guidance or colour on your estimated cash burn for this year?

And second question, how confident are you in obtaining the first results from THR-409 by the end of 2017? I believe it was originally planned second half 2017. That's, I assume, due to the protocol changes to speed up the recruitment, but how confident are you that you're going to reach that goal to be able to show results year-end 2017? Thank you.

**Patrik De Haes:** So, as mentioned before, the protocol changes had a positive impact on the recruitment rate. What we basically did with the protocol change is we allowed less severe patients with the non-proliferative form. And what we see is that the discrete failure rate went down with 50%, so that gives us a certain confidence that we're going to speed up the study. So, this is, as I say, the first two months after that protocol change; we're going to have to monitor that, whether that increased rate of inclusion continues, in order to make sure that we can commit to that reading-out of the study in the timeline mentioned. Dominique, for the other question?

**Dominique Vanfleteren:** Yeah on the cash burn, I think like previous years, the bracket is between €20–30 million depending on how much we're capable of implementing in time. You have seen that we had the same bracket last year, and you see that the cash burn has been very, very low; I mean, lower than €30 million. So, that might indicate that this year we will have to take some activities, and it might be closer to €30 million than to €20 million.



**Operator:** Thank you very much. We have no further questions for the moment.

**Patrik De Haes:** Okay, there's nothing now, we can conclude.

