

# ThromboGenics

ThromboGenics

Annual Report

2008



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## Annual Report 2008

### **ThromboGenics' Mission**

«ThromboGenics develops innovative vascular biopharmaceuticals, while applying the highest scientific and ethical standards, to create sustainable value for all of its stakeholders.»

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# I. About ThromboGenics

## Company profile



ThromboGenics NV (Euronext Brussels: THR) is a leading European biotechnology company focused on the discovery and development of novel biotherapeutics for a number of important therapeutic areas including back of the eye disease, vascular disease and cancer.

ThromboGenics' most advanced product is microplasmin, which

has already shown the potential to resolve certain back of the eye conditions, resulting in an improvement in the patient's vision and potentially avoiding surgical procedures. In a key development for the Company, microplasmin began its Phase III clinical program in early 2009. This Phase III program is designed to demonstrate that microplasmin is effective in treating certain eye diseases caused by vitreomacular adhesion, a condition when the vitreous (the central gel part of the eye) has an abnormally strong adhesion to the surface of the back of the eye (the retina).

ThromboGenics intends to file the data from this Phase III program with the regulatory authorities in 2011 to gain approval to market the product in both the U.S. and Europe.

ThromboGenics plans to market microplasmin itself and to use this promising new

product to build a successful franchise in ophthalmic medicine.

The Company has made this decision based on the commercial potential of microplasmin and the well defined group of prescribing doctors that will use the product. ThromboGenics is

partnering opportunities.

In 2008, ThromboGenics announced a large out-licensing deal with Roche for its anti-cancer antibody, TB-403 (anti-PLGF). This deal, which could be worth up to € 300 million to the Company in upfront and milestone payments, plus future double digit royalties, has provided the financial resources

a potential partnering deal for this exciting new product. The Company is also looking for a partner to continue the development of microplasmin for the treatment of stroke.

ThromboGenics currently has partnering deals with a number of international companies, including Roche, BioInvent, Bharat Biotech International and Rhein Minapharm. The Company also continues to capitalise on its strong links to both Belgian and international academic institutions as it seeks to build its earlier stage pipeline.

In 2008, ThromboGenics moved into its new headquarters building. This new facility, which will house all of the Company's staff in Belgium, will allow ThromboGenics to continue to capitalise on its excellent scientific heritage, rich academic culture, and world-class in-house expertise.

## **“ ThromboGenics NV is a leading European biotechnology company”**

currently looking for additional late stage ophthalmic product opportunities to further strengthen its position in this attractive market. The Company's decision to commercialise microplasmin by itself is also based on its solid financial situation. This is in part due to the funding that the Company has generated from the licensing deal for its novel antibody TB-403, and the value to be derived from future

needed to invest in the further development of microplasmin and other opportunities. ThromboGenics is currently conducting a large Phase II clinical trial with TB-402 (anti-Factor VIII), a novel long acting anti-coagulant which is being developed to prevent thrombosis after surgery and atrial fibrillation. The data from this study will form a key element of the package that the Company will use to sign

## Highlights

### January 18, 2008

ThromboGenics and co-development partner BioInvent receive approval from the regulatory authorities in Denmark to initiate a Phase I clinical trial of the novel anti-cancer agent TB-403.

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### April 1, 2008

ThromboGenics announces the completion of patient enrolment for its Phase IIb MIVI III trial in the United States. This study evaluated the safety and efficacy of Microplasmin in vitrectomy.

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### April 9, 2008

ThromboGenics completes patient enrolment for its Phase II MITI IV study. The primary purpose of this study was to evaluate the safety and preliminary efficacy of microplasmin when administered intravenously to acute stroke patients between four and twelve hours after the onset of the stroke.

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### May 23, 2008

ThromboGenics presents further results of the Vitreomacular Traction Trial (MIVI IIT) at the

Euretina Annual Meeting in Vienna. Results confirm the beneficial effects of microplasmin in patients with vitreomacular traction, including macular holes, without need for vitrectomy throughout the 6 month follow-up period. Specifically, the microplasmin 125 µg dose safely induced resolution of vitreomacular traction without the need for surgical intervention in over 40% of patients.

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### June 3, 2008

ThromboGenics and BioInvent report positive Phase Ia results for anti-PLGF cancer therapeutic TB-403. Approval is also received to start a second repeat-dose Phase Ib study in patients with advanced cancer.

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### June 18, 2008

ThromboGenics and BioInvent sign a strategic alliance with Roche for TB-403, the novel anti-cancer antibody. Under the terms of the agreement, ThromboGenics and BioInvent receive an upfront payment of € 50 million. In addition, ThromboGenics and BioInvent could potentially receive up to € 450 million over the term of the collaboration based on the successful completion of a series of development and commercial milestones for

multiple indications, as well as double digit royalties on potential product sales. ThromboGenics, which discovered TB-403, will receive 60% and BioInvent 40% of the revenue from the deal.

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### June 30, 2008

ThromboGenics reports positive results from its Phase IIb Trial of Microplasmin in Vitrectomy (MIVI III). The results confirm microplasmin's potential to make a major contribution to the treatment of back of the eye disease, with the highest (125 µg) dose of microplasmin safely inducing a PVD (Posterior Vitreous Detachment) in approximately 30% of patients within 1 week of treatment, without the need for surgical intervention.

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### July 30, 2008

ThromboGenics announces that a group of private investors based in Belgium have together acquired an 8% stake in the Company.

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### August, 2008

ThromboGenics moves to a new, more spacious headquarters at the 'Bioincubator' park in Leuven, Belgium. The



new facility enables all of ThromboGenics' staff in Belgium to work in one location in a modern, state-of-the-art building.

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#### August 28, 2008

ThromboGenics appoints Dr. Patrik De Haes to succeed Professor Désiré Collen as the Company's new Chief Executive Officer.

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#### September 19, 2008

ThromboGenics is promoted to the Belgian Midcap Index, reflecting the significant progress the Company has made since its IPO in 2006.

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#### September 29, 2008

ThromboGenics announces promising results from the MITI IV Phase II trial of microplasmin for the treatment of acute stroke. The results of the study are presented at the World Stroke Congress.

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#### November 14, 2008

ThromboGenics announces promising six month follow-up results from its Phase IIb trial of Microplasmin (MIVI III) for

treatment of visual disorders. The results continue to support microplasmin's potential to make a major contribution to the treatment of back of the eye disease.

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#### January 9, 2009

ThromboGenics announces the start of the Phase III clinical program of microplasmin for the non-surgical treatment of back of the eye disease. Microplasmin's pivotal Phase III program is referred to as MIVI-TRUST (Microplasmin for IntraVitreous Injection-Traction Release without Surgical Treatment).

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#### January 26, 2009

ThromboGenics and BioInvent receive a technology transfer success fee of € 5 million from Roche under the terms of their strategic alliance for the novel anti-cancer antibody, TB-403.

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#### February 20, 2009

ThromboGenics approves a cross-border merger of subsidiaries into parent company ThromboGenics NV.

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#### February 23, 2009

ThromboGenics and BioInvent announce the start of the Phase II trial of the novel, long acting anticoagulant, TB-402 for the prophylaxis of Deep Vein Thrombosis (DVT) following orthopaedic surgery.

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#### February 27, 2009

ThromboGenics is awarded a € 3.2 million grant for the development of its Anti-VPAC1 antibody for cancer chemotherapy induced thrombocytopenia from the Institute for the Promotion of Innovation by Science and Technology in Flanders (IWT).

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#### March 6, 2009

ThromboGenics announces completion of patient enrolment for the Phase II trial of microplasmin intravitreal injection for the treatment of Diabetic Macular Edema (MIVI II DME). This trial is designed as the initial step in evaluating the utility of microplasmin in patients with diabetes, a group which is more prone to eye disease such as diabetic retinopathy, due to their underlying medical condition.

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Competent people,  
efficient team work,  
knowledge and experience...

for great results

«2008 was a transformational year for ThromboGenics,  
when we started to emerge as one of the leading  
biotechnology companies in Europe.»

Patrik De Haes, CEO





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## 2. Interview with the Chairman and CEO of ThromboGenics

**Patrik De Haes, CEO,  
and Désiré Collen,  
Chairman, discuss  
the achievements of  
ThromboGenics in 2008,  
and their aims for the  
future:**

### **1. How would you describe 2008 for ThromboGenics?**

**PATRIK:** 2008 was a transformational year for ThromboGenics, when we started to emerge as one of the leading biotechnology companies in Europe. This transformation was based on two key developments. In June, we signed a highly valuable licensing deal with Roche for the clinical development and commercialisation of our novel anti-PIGF antibody TB-403. We also generated exciting Phase II clinical data with microplasmin for the non-surgical treatment of back of the eye disease, which demonstrated the potential value of the product.

These key events, coupled with the additional funding that we have received and anticipate receiving from Roche, has allowed us to begin the Phase III development of microplasmin on an independent basis.

Starting this Phase III program is a major milestone for the Company. Our success has also led to our shares being included in the Bel Mid Cap index from October onwards. Our aim continues to be to build a strong, value driven company, focused on innovative products to treat areas of unmet medical need. I fully expect ThromboGenics to continue to make progress toward this goal in 2009 and beyond.

### **2. What are your views about 2008 for ThromboGenics?**

**DÉSIRÉ:** 2008 was about continuity through change for ThromboGenics. We have modified our strategy to place greater emphasis on microplasmin in eye disease, we have strengthened our organisation, and we have moved to a new facility to ensure we can operate more efficiently. We continue to work on developing our pipeline and seeking out new

pre-clinical opportunities based on our international networks. We have also made a very orderly, well planned management transition, with Patrik taking over from me as the Company's CEO. I am confident that this important change and the overall strength of our organisation will allow ThromboGenics to continue to make the excellent progress that we have seen since our IPO in 2006.

**3. Can you tell me more about your microplasmin and eye disease program and why you are so confident of its success?**

**PATRIK:** Microplasmin is a novel product that represents a unique approach to treating important back of the eye diseases. It is our hope that patients who are treated in a single office procedure with microplasmin could achieve resolution of their underlying back of the eye disease without the need for major



Désiré Collen, Chairman and Patrik De Haes, CEO

eye surgery. This belief is based on the very encouraging Phase II data we have reported with microplasmin. These studies have shown that microplasmin was able to resolve the underlying disease in a significant number of patients, without the need for surgery. Equally important is that this disease resolution was accompanied by a marked

improvement in the patient's vision.

We believe that microplasmin has the potential to have a significant impact in the treatment of many back of the eye diseases. The very promising data we have generated to date, the limited competition and the large potential market has given

us the confidence to take this unique product further using our own resources. This has the further advantage of allowing us to retain much more of the potential upside for ThromboGenics. I am looking forward to reporting the results of the current Phase III program with microplasmin for the non-surgical treatment of vitreomacular adhesion by the end of 2010.

**4. Can you tell me more about the development programs of your novel antibodies TB-402 and TB-403, and how your R&D efforts are focused to produce more products of their caliber?**

**PATRIK:** We are very pleased with the achievements we have made with the novel anti-cancer agent TB-403 during 2008. Signing the deal with Roche in June provided us with 60% of a € 50 million up-front payment, and 60% of a potential further € 450 million from a range of milestones. This has given

the Company much greater strategic flexibility and a sound financial footing. This stronger financial position has allowed us to more actively invest in building the value of our exciting pipeline.

It is also our aim to conclude a significant licensing deal for TB-402, a human antibody currently in Phase II clinical trials. We have decided to partner this product because of the investment needed to both develop and commercialize TB-402, an anti-coagulant targeting very large markets. Pre-clinical and clinical work to date has shown that TB-402 is a unique, long acting agent that could offer real benefits in the prevention of potentially life threatening conditions such as thrombosis after surgery and atrial fibrillation. The commercial opportunity we are targeting with TB-402 is potentially very large. In the U.S. alone, it is estimated that more than 350,000

individuals are affected by DVT or pulmonary embolism (PE) each year<sup>1</sup>. We have recently begun a Phase II trial with TB-402 for prevention of DVT in patients who have undergone orthopaedic surgery. Data from this study, which is due to complete toward the end of 2010, are designed to help us achieve our aim of securing a licensing deal with a major pharmaceutical partner.

**DÉSIRÉ:** I am very happy that the potential we saw a few years ago in both TB-403 and TB-402 is being increasingly recognized. These two novel antibodies clearly demonstrate the strong scientific heritage we are able to access and cultivate here at ThromboGenics. We are committed to further building our links with research centers and universities, both in Belgium and internationally, with the aim to strengthen our product portfolio by capturing some of the best pioneering research globally available. We

1. "The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism," September 15, 2008, p.1.

are now able to better handle new pre-clinical projects, given our move into our own R&D facility and the strengthening of our development organisation. I am sure we will be able to announce a number of exciting additions to our pipeline in due course.

**5. What are your plans for ThromboGenics in the future and what significant milestones can we expect to see in the next 12-18 months?**

**PATRIK:** We are very much focused on delivering the corporate milestones that will generate the most value for our shareholders. We are also working to position ourselves as one of the leading biotech companies globally.

Against this background, our key targets are to ensure smooth and rapid patient recruitment into the Phase III clinical program with microplasmin in eye disease, and our on-going Phase II study

with TB-402 in orthopaedic surgery patients. We will also continue to build our productive working relationship with Roche and BioInvent, as we continue the development of TB-403. We anticipate further important financial milestones from Roche as the product moves through clinical development and towards the market.

A final key objective is to capitalize on our global links with academia to ensure that we can add cutting edge biotherapeutics to our pre-clinical pipeline. Discussions are on-going with a number of parties and we expect to be in a position to announce a deal in this area within the next 12 months.

**6. How is ThromboGenics positioned to withstand the global credit crisis?**

**DÉSIRÉ:** I believe that we are well positioned to prosper in what is clearly a difficult economic environment. We have

sufficient cash to support our operating activities over the next two years. In addition, we have the opportunity to generate further financial resources as a result of milestone payments from Roche and a potential licensing deal on our unique anti-coagulant, TB-402. Our business is run very efficiently, with a clear focus on translating early stage ideas into strong commercial opportunities, using our scientific, clinical and business development expertise.

Given these positives and the growing evidence that products such as microplasmin and TB-402 could make significant difference in their respective therapeutic areas, I am confident that ThromboGenics will be able to generate significant value over the next 18 months, despite the current depressed financial situation.

Efficient products,  
a strong pipeline,  
experienced staff,

for a better future

«Seeing the clear clinical benefits of a truly innovative  
eye medication such as microplasmin is very exciting.»»

Prof. Dr. Peter Stalmans







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### 3. Key Development Programs

#### Microplasmin – Building an Ophthalmic Franchise



Microplasmin is an exciting product which has the potential to transform the treatment of a number of important back of the eye diseases. Given this potential, ThromboGenics is currently investing considerable resources in both the clinical development and pre-commercialization activities for microplasmin, with the ultimate aim of building an ophthalmology franchise. Microplasmin's Phase III clinical program began in early 2009.

Excitement around microplasmin is due to its unique mode of action, the positive clinical results

that have been seen to date, and the tremendous unmet need that exists for the range of indications that this product is targeting. A further potential positive is that microplasmin could be used for many patients, as a one-off treatment delivered in the doctor's office.

Microplasmin could represent a highly significant departure from the way we presently treat back of the eye diseases. Current treatment for many of these conditions requires the separation of the vitreous (the gel-like substance in the center of the eye) from the retina, which plays a crucial role in vision. This separation is called a posterior vitreous detachment (PVD). PVD is potentially beneficial in several back of the eye diseases including macular hole, diabetic retinopathy, diabetic macular edema and age-related macular degeneration. Currently, PVD is achieved via a surgical procedure called vitrectomy,

which involves the complete removal of the vitreous using suction. This procedure is costly and a proportion of patients experience side effects, which include alteration of vision, bleeding, retinal detachment, and development of glaucoma and cataracts.

A one-off treatment with microplasmin is expected to eliminate the need for surgery in many patients. This is because microplasmin dissolves the protein formations that link the vitreous to the retina. In clinical trials to date, 30-40% of patients experience a PVD when treated with microplasmin without the need for surgery. In many of the remaining patients, the surgical procedure is made easier because the links between the vitreous and the retina have been weakened. Microplasmin could therefore provide a safer and more effective method of inducing a PVD, either alone or in combination with surgery.



## **The Microplasmin Phase III Program**



ThromboGenics has continued to report positive results, as it has pressed ahead with the development of microplasmin for eye disease, throughout 2008. Following a successful “End of Phase II meeting” with the FDA, ThromboGenics began preparations for the final step in the clinical development of this potential new therapy: the pivotal Phase III clinical program with microplasmin for the non-surgical treatment of back of the eye diseases.

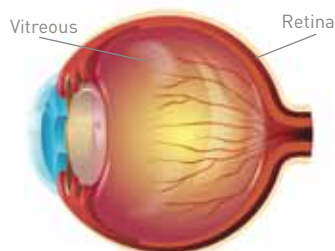
The start of the Phase III clinical program represents a major

milestone in the Company’s development. The program involves two clinical trials, taking place in the United States (TG-MV-006 trial) and in Europe and the United States (TG-MV-007 trial). The initial indication for both of the Phase III microplasmin trials is the non-surgical treatment of focal vitreomacular adhesion. Vitreomacular adhesion is a condition in which the vitreous gel, in the center of the eye, has an abnormally strong adhesion to the retina at the back of the eye. These adhesions can cause vessel and retinal distortion which results in deterioration in the patient’s vision. Moreover, vitreomacular adhesion is thought to play a key role in numerous back of the eye conditions such as macular hole formation, and some forms of macular edema. Both trials are multi-center, randomized, placebo controlled, double-masked studies which will evaluate 125 µg of microplasmin versus placebo in the intravitreal treatment of patients with focal vitreomacular adhesion.

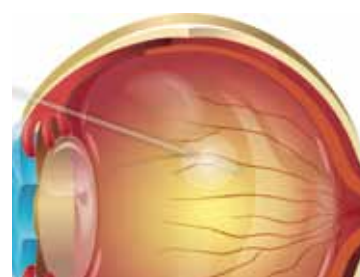
Each trial will enrol approximately 320 patients across approximately 40 centers in the United States (TG-MV-006) and 40 centers in Europe and North America (TG-MV-007). The primary endpoint of both trials is the non-surgical resolution of focal vitreomacular adhesion after one month. Additional measures of efficacy and safety will also be assessed at various intervals over six months in both studies. It is estimated that these two studies will be completed by the end of 2010.

In parallel to the Phase III development of microplasmin, ThromboGenics will begin the pre-commercialization activities needed to successfully bring microplasmin to the market. These activities, combined with the significant market opportunity in eye disease, provide ThromboGenics with an outstanding platform to begin to build an ophthalmology focused franchise which will target both the U.S. and European eye disease markets.

1. CROSS SECTION OF THE EYE



2. MICROPLASMIN IS INJECTED INTO THE VITREOUS



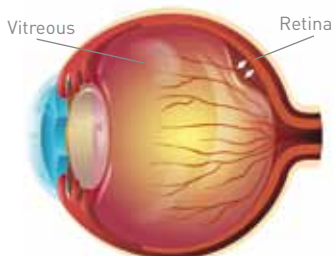
3. THE VITREOUS IS ATTACHED TO THE RETINA VIA A «MOLECULAR GLUE»



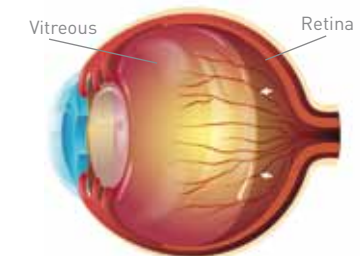
4. MICROPLASMIN ACTS ON THE «MOLECULAR GLUE» BREAKING IT DOWN



5. THE VITREOUS BEGINS TO SEPARATE AWAY FROM THE RETINA



6. FULL SEPARATION OF THE VITREOUS FROM THE RETINA IS ACHIEVED



## Exciting Clinical Results Throughout 2008



The significant progress that ThromboGenics has made in developing microplasmin was highlighted by the string of positive results, both in terms of efficacy and safety, that were announced during 2008. In May, further results from the Vitreomacular Traction Trial (MIVI IIT) were presented at the Euretina Annual Meeting in Vienna. The study confirmed the beneficial effects of microplasmin treatment in patients who had been followed for a period of 6 months post treatment. In this

study, 11 of the 25, or 44%, of the microplasmin (125  $\mu$ g) treated patients saw a resolution of their vitreomacular traction (including macular hole closure in 2 of the 4 macular hole cases) without the need for vitrectomy. The trial was a sham injection controlled study in which patients were assigned to receive either placebo, 75  $\mu$ g or 125  $\mu$ g of microplasmin.

Following these encouraging results, ThromboGenics began the MIVI III trial, which was designed to evaluate the safety and efficacy of microplasmin in patients who were scheduled to undergo a vitrectomy. The trial was a Phase IIb, randomized, double-masked, placebo-controlled, dose-ranging trial evaluating three doses of microplasmin (25, 75 and 125  $\mu$ g) versus placebo in 125 patients. The trial showed that the most effective dose of microplasmin studied (125  $\mu$ g) was able to resolve the underlying disease in approximately 30% of patients without the need for vitrectomy.



The visual acuity of all of the patients recruited into this study was also measured at day 35 after the injection of microplasmin or placebo, whether they had a vitrectomy or not. In patients who received the 125 µg dose of microplasmin there was an improvement in vision (6.9 more letters read on a standard eye chart compared to a baseline reading prior to treatment); this compares with a 4.7 letter improvement for all microplasmin treated patients and a 0.1 letter improvement for the placebo group.

Further results from this study, including six month follow-up data, were reported at the American Academy of Ophthalmology in Atlanta, USA in November, 2008. These results showed that all of the patients in the trial who at 1 month had achieved complete resolution of their vitreomacular traction or macular hole without need for surgery had not experienced a recurrence of

either traction or macular hole during the full 6 month follow-up period.

The six month results also show that these patients continue to see an improvement in their visual acuity. Importantly, this improvement in visual acuity is at least as good as the results

**“The significant progress that ThromboGenics has made in developing microplasmin was highlighted by the string of positive results, both in terms of efficacy and safety, that were announced during 2008.”**

seen in patients who had to undergo a surgical vitrectomy in order to resolve their underlying eye disease. These results, along with the similar findings observed in the MIVI II Traction trial, represent the first ever demonstration of a drug based treatment option for these conditions that would otherwise have required major eye surgery.

## Diabetic Retinopathy



**“ThromboGenics is currently investigating the use of microplasmin in the treatment of diabetic retinopathy .”**

ThromboGenics intends to develop microplasmin for a broad range of back of the eye diseases. The Company is currently investigating the use of microplasmin in the treatment of diabetic retinopathy and has recently completed the enrolment of patients in a Phase II trial

for the treatment of Diabetic Macular Edema (DME). Diabetic retinopathy is a major cause of visual loss and the leading cause of blindness in patients aged 20-60. Diabetic Macular Edema (DME) is a condition where swelling of the retina occurs in patients with diabetic retinopathy, due to a leakage of fluid from blood vessels within the macula.

The MIVI II DME trial is a Phase II, randomized, double masked, sham injection controlled, ascending dose clinical trial evaluating the safety and initial efficacy of intravitreal microplasmin for the treatment of patients with Diabetic Macular Edema.

This initial study is an important first step in evaluating microplasmin's effect in the diabetic retinopathy population in general. Results are expected to be presented towards the end of 2009.



### **TB-402 – A Unique Partnering Opportunity**

TB-402 is a novel antibody being developed by ThromboGenics as an anti-coagulant to prevent unwanted thrombotic events. Clinical and pre-clinical studies have already shown that TB-402 has unique properties that could provide important advantages in the prevention of important coagulation disorders, including deep vein thrombosis, post surgery, and atrial fibrillation.

ThromboGenics intends to out-license TB-402 to a partner with the scale and financial resources needed to complete the late stage clinical development of TB-402 and to ensure its commercial success, given the size of markets which it is targeting. TB-402 is a novel anticoagulant agent, which is expected to deliver important clinical benefits due to it only partially inhibiting Factor VIII activity, even when

given in very high doses. Factor VIII is an important component of the blood clotting cascade. This novel mode of action is expected to reduce the risk of undesirable bleeding events and the need for patient monitoring, the two main drawbacks associated with current anticoagulants. Furthermore, TB-402 is a long-acting agent which

would mean that after surgery, patients would only require a single dose. Importantly, the effects of TB-402 are reversible, meaning that patients who have received TB-402 could have further surgery if this suddenly became necessary. TB-402, like TB-403, is being developed with BioInvent.



## Deep Vein Thrombosis

ThromboGenics has recently started a Phase II trial of TB-402 for the prophylaxis of Deep Vein Thrombosis (DVT) following orthopaedic surgery. DVT is caused when a blood clot forms in a deep vein, most commonly in the lower leg. As underlined by a recent Call to Action by the U.S. Surgeon General, DVT is deemed to be a major public health issue. It is estimated that in the U.S. alone, more than 350,000

**“ It is estimated that in the U.S. alone, more than 350,000 individuals are affected by DVT or pulmonary embolism (PE) each year.”**

individuals are affected by DVT or pulmonary embolism (PE) each year. Moreover, DVT and PE together may be responsible for more than 100,000 deaths in the U.S. each year.

Equally important is that the market opportunity for TB-402 is growing; it is estimated that by 2015, 1.4 million patients will undergo knee replacement and 600,000 patients will undergo

hip replacement in the U.S. if current trends persist<sup>1</sup>. Patients undergoing hip replacement or knee surgery are particularly at risk of developing DVT, and all patients are therefore treated with anticoagulants prophylactically in order to reduce the risks of blood clots. Given this large and growing market opportunity for TB-402 and the sales reach that will be needed to engage potential prescribers, ThromboGenics intends to seek a partner to undertake the later stage development and commercialization of this exciting new agent.

The current Phase II trial is an active (enoxaparin)-controlled, dose-escalating, multicenter, prospective, randomised, open label trial. The study will assess three different doses of TB-402 given as a single intravenous bolus injection post knee replacement surgery. The trial will enrol 300 patients across 36 centers mainly in Central Europe. The primary endpoint is the safety and efficacy of the three escalating doses of TB-402, and it is anticipated that this study will conclude by the end of 2010.

1. "Changes in Surgical Loads and Economic Burden of Hip and Knee Replacements in the US: 1997-2004," Sunny Kim, Arthritis & Rheumatism (Arthritis Care & Research), April 15, 2008; 59:4, pp. 481-488.

## The Current Anti-Coagulant Market – the Drawbacks

The anti-coagulant market is currently worth over \$5 billion per annum globally. The market is predominantly split between the oral treatment warfarin and the injectable heparin; however, there are a number of acknowledged drawbacks with these therapies.

Warfarin is the most frequently prescribed oral anti-coagulant, with annual sales of approximately \$500 million<sup>3</sup>. However, there are significant problems with warfarin therapy. It has numerous drug-drug interactions and common food-drug interactions, which can often result in unpredictable dosage response. This means that patients receiving warfarin require continuous monitoring, which is very costly and inconvenient. Moreover, warfarin has numerous side effects, the most significant of which is that it can cause severe hemorrhage.

Sanofi-Aventis' Lovenox (enoxaparin), a low molecular

weight product, dominates the heparin market, generating sales of \$3.3 billion in the top seven markets in 2006<sup>4</sup>. Lovenox also has a number of drawbacks, including the need for it to be injected on a daily basis, which is not ideal from a patient's perspective. It can, on occasion, also cause spontaneous bleeding events.

Current anti-coagulant drug development is mainly focused on oral agents, particularly Factor Xa inhibitors. Although these products are oral, they still suffer from a number of drawbacks,

including frequent dosing and the fact that they are not reversible. This means that although TB-402 will come to market following the introduction of the new oral Factor Xa agents, it is still expected that TB-402 will assume an important place in the anti-coagulant market. This is due to TB-402's long-acting properties, which means it offers additional advantages by ensuring safe anti-coagulation for up to one month with a single dose.

Set against this backdrop, TB-402's novel mode of action is highly compelling.



3.«Retail perspective and provider perspective audit. Plymouth Meeting, Pa.: IMS America, 1998.»

4. Commercial Insight: Antithrombotics, Datamonitor (October 2007).

## Atrial Fibrillation



Another area where TB-402 could have significant potential is in Atrial Fibrillation (AF). AF is a heart arrhythmia caused by the upper chambers of the heart beating irregularly. This can result in blood not being fully pumped out of the heart,

leading to the formation of blood clots, which have the potential to cause a stroke if they travel to the arteries supplying the brain. AF is becoming increasingly frequent in elderly patients and affects approximately 7 million people in Europe and the United States. TB-402's novel anti-coagulant characteristics could therefore be an important treatment in AF sufferers to prevent stroke.

## Roche Licenses TB-403 (Anti-PIGF) – A Key Strategic Event

In June 2008, ThromboGenics made the strategic decision to sign a major partnership deal with Roche for its unique anti-cancer agent TB-403. TB-403 is a potential breakthrough in the treatment of cancer.

This exciting potential is based on the ability of TB-403 to selectively inhibit the formation of the new blood vessels that are needed to support the growth of cancer tissue.

ThromboGenics and its co-development partner BioInvent received an upfront payment of € 50 million, with an additional € 450 million in potential milestones, as well as double digit royalties on future product sales. The working relationship with Roche is progressing well, and in February 2009 ThromboGenics and BioInvent received a technology transfer success fee of € 5 million. ThromboGenics, who discovered TB-403, receives 60% and BioInvent 40% of all revenue from the Roche deal.

The financial payments from the TB-403 deal with Roche have allowed ThromboGenics to invest in the clinical programs the Company believes will have the highest impact on its corporate development, and will create the most value for its shareholders. ThromboGenics has not only been able to fund its own Phase III program for its lead product microplasmin, but also to

investigate the potential of this product in a broader range of back of the eye indications.

TB-403 is a humanized monoclonal anti-PIGF (placental growth factor) antibody that blocks the formation of new blood vessels in solid tumors. By blocking the formation of new blood vessels (anti-angiogenesis), TB-403 has the potential to reduce the growth and spread of cancer cells.

Scientists have been aware of the benefits of angiogenesis inhibitors on reducing tumour size; however, current angiogenesis inhibitors, though they work to inhibit the growth of the formation of new blood vessels, do so in both cancerous and healthy tissue. Their therapeutic potential therefore is hampered by side effects. TB-403 can inhibit the growth of new blood vessels in cancer tissue, but do so without having any effect on healthy tissue.

In early June 2008, ThromboGenics announced positive Phase Ia results for TB-403. The results showed that TB-403 was safe and well tolerated, with pharmacokinetic properties enabling it to be developed for the treatment of cancer. TB-403 is currently in a Phase Ib trial which will evaluate the tolerability, pharmacokinetics and pharmacodynamics of TB-403 in patients with advanced cancer.

On the signing of the deal, Roche assumed responsibility for all future development costs for TB-403, including the costs of the on-going Phase Ib trial which is currently being run by ThromboGenics and BioInvent. ThromboGenics and BioInvent in conjunction with Roche have formed a Joint Steering Committee, to oversee the future research and development activities for TB-403.

Working with passion,  
strong partnerships,  
ongoing research...

for quality products

«Seeing microplasmin dissolve older, more difficult to  
treat, blood clots in 'stroke' patients is impressive.»

Prof. Dr. Vincent Thijs







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## 4. Other Development Programs

### Microplasmin for the Treatment of Stroke



ThromboGenics has also been developing microplasmin for the treatment of vascular diseases, specifically for the treatment of acute ischemic stroke.

Microplasmin plays a key role in dissolving blood clots, such as those that cause acute ischemic

stroke. It is a direct-acting thrombolytic agent that has the potential to restore blood flow efficiently within an extended period after a stroke event, possibly up to 12 hours, and has potentially fewer side-effects than other thrombolytic agents.

Results from a Phase II study of microplasmin for the treatment of acute stroke, presented at the World Stroke Congress in Vienna in September 2008, showed that microplasmin not only was generally well tolerated, but also produced some interesting efficacy results. Approximately 25% of patients treated with microplasmin had reperfusion (restoration of blood flow) within eight hours of being treated, compared with 10% of placebo-treated patients. Moreover, of the patients who had experienced more severe vascular blockages, 33% of patients treated with microplasmin achieved

reperfusion, compared with 14% of placebo-treated patients. Due to the small size of the study, neither of these end points were statistically significant.

The study also showed that microplasmin-treated patients had a statistically significant lower level of damage to the blood brain barrier compared to placebo-treated patients, measured using the marker of matrix metalloproteinase (MMP). MMP activation plays a crucial role in the pathogenesis of brain edema and hemorrhagic transformation after ischemic stroke.

After reporting these promising results from Phase II trials with microplasmin, ThromboGenics has decided, due to the costs and risks involved in developing new products for stroke, that it will only continue development of this interesting product in conjunction with a partner.



## **Staphylokinase**

Staphylokinase is a thrombolytic agent that could be used in cardiovascular disease to dissolve blood clots. Development of staphylokinase is focused on the treatment of acute myocardial infarction (AMI), commonly known as a heart attack.

Staphylokinase has been shown in Phase II trials to potentially have comparable efficacy to tissue plasminogen activator or tPA, which is the most commonly used thrombolytic to treat heart attacks in wealthier economies. However, staphylokinase can be made available to patients at a much lower cost.

Given these characteristics, and the high cost of the clinical studies needed to gain approval in the regions where tPA is marketed, development of staphylokinase is being targeted at the developing world.

## **THR-100**

In 2006, ThromboGenics entered into an agreement with Bharat Biotech International Ltd. (India) for the clinical development, manufacturing and commercialisation of THR-100 (Staphylokinase). Under the terms of the agreement, ThromboGenics will receive double-digit royalties on net sales and Bharat Biotech will assume responsibility for all future costs. Bharat Biotech has the capability to produce staphylokinase, and is currently in discussion with the regulatory authorities in India about starting the product's further clinical development.

## **THR-174**

THR-174 is a second generation form of staphylokinase, which has the potential to demonstrate a better efficacy and safety profile. This is in part due to its reduced immunogenicity compared to earlier versions of staphylokinase and other established thrombolytics, in the developing world, such as streptokinase.

In 2007, ThromboGenics signed a license agreement with Rhein Minapharm (Egypt) for the production, clinical development and commercialization of THR-174 in the Middle East, Africa and other countries. In return for granting this license, ThromboGenics will receive upfront and milestone payments, and will earn double digit royalties on net sales, while Rhein Minapharm will assume responsibility for all future costs.



A strong pipeline,  
well equipped facilities,  
competent staff...

for maximum added value

« I believe we are writing a new chapter in cancer  
treatment, with TB-403 (anti-PlGF ). »

Prof. Dr. Peter Carmeliet





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## 5. Research and Development

### Strategy



ThromboGenics' business success is based on the ability to access cutting edge science and translate it into products which address areas of significant unmet medical need. ThromboGenics has built up a very strong network of potential partners both in Belgium and internationally so that it can access the truly innovative science and technology projects that it needs to generate significant value for its shareholders. Products that are now part of its clinical development pipeline have been sourced from leading Belgian

institutes, the University of Leuven and the Flanders Institute for Biotechnology (VIB).

The Company has recently moved to its own dedicated headquarters facility. This new facility has allowed the Company to bring all of its scientists under one roof creating an even more focused and united approach to its R&D activities. It will also enable the Company to continue to develop and broaden its unique product pipeline.

ThromboGenics is currently in discussions with a broad range of research centers and Universities across Belgium and internationally to gain access to technology and molecules that will act as a starting point to further build its pre-clinical pipeline. Based on the discussions it has held to date, the Company is confident that it will be in a position to initiate new high quality projects during the latter part of 2009.



## Anti-VPAC

ThromboGenics has recently announced that it has been awarded a grant of up to € 3.2 million for the continued development of its Anti-VPAC1 (**V**asoactive Intestinal Peptide/**P**ituitary **A**denylyl **C**yclase-Activating Peptide Receptor **1**) antibody for the treatment of thrombocytopenia (low platelet count).

The grant represents an important source of funding to support the development of this novel product, which is expected to begin clinical trials in 2011.

A common, severe side-effect of chemotherapy in cancer patients is thrombocytopenia. This is when the number of platelets in the patient's blood is lower than normal. The patient is then at risk of bleeding and severe hemorrhage because low platelet count prevents their



blood from clotting normally. This is a significant clinical problem, as in some patients it can lead to the discontinuation of their cancer treatment. The current standard of care for chemotherapy-induced thrombocytopenia is a blood platelet transfusion; however,

**“Thrombocytopenia is a significant clinical problem, as in some patients it can lead to the discontinuation of their cancer treatment”**

this only offers a temporary solution and is associated with further cost and risks. There is therefore a clear need for a product that is able to accelerate the patient's platelet production.

Research undertaken by ThromboGenics in conjunction with the University of Leuven has shown that the inhibition of VPAC1-mediated signalling

could stimulate the production of platelets. The VPAC1 receptor is present at the surface of bone marrow cells called megakaryocytes, which, when mature, produce platelets. Recent findings published in the journal for the American Society of Hematology, Blood, has indicated that the inhibition of VPAC1 promotes megakaryocyte maturation and therefore could constitute a novel strategy to increase a patient's platelet count and functionality after chemotherapy treatment.<sup>1</sup>

The grant has come from the Institute for the Promotion of Innovation by Science and Technology in Flanders (IWT) and is based on the successful completion of a series of development milestones over the next three years. IWT is a public institution created by the Flemish government to provide R&D and innovation support to projects based in Flanders.

1. "PACAP and its receptor VPAC1 regulate megakaryocyte maturation: therapeutic implications." Freson, Peeters, De Vos, Wittevrongel, Thys, Hoylaerts, Vermeylen and Van Geet, Blood, 111(4):1885-93 (2008)



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## 6. Company Organization

# Human Resources

### Main Events during 2008



Over the last twelve months, ThromboGenics has continued to demonstrate why it is one of the more exciting biotechnology

companies in Europe. Excellent progress with the Company's clinical pipeline and major licensing deal with Roche for its novel anti-cancer antibody TB-403 highlighted the strengths of the ThromboGenics' team. ThromboGenics' success is based on its excellent scientific heritage, rich academic culture, and world-class in-house expertise.

Recent progress means that ThromboGenics remains on track to build a strong, value-driven company focused on innovative products for areas of unmet medical need. ThromboGenics is confident that it will continue to create further shareholder value in 2009 and beyond.

In September, ThromboGenics made a seamless senior management transition with **Patrik De Haes** becoming the Company's new Chief Executive

Officer. He had previously been the Company's Chief Operating Officer. He succeeded the Company's founder, **Désiré Collen**, who remains the Chairman of the Board. The Company is set to continue to prosper under his leadership as his transition from COO to CEO reflects the organization's continuity at the senior management level.

Patrik has considerable international experience across the biotechnology and healthcare sectors spanning more than 20 years, with a background in development and commercialization. During his period as Chief Operating Officer, he was heavily involved in delivering a number of transforming milestones for ThromboGenics and has also been a major contributor to the Company's evolving business strategy.

In the development of its operations and management team, ThromboGenics has hired additional professional talent. In July 2008, **Andy De Deene** was recruited to join the management team as Head of Program Management. Andy brings to the Company considerable experience in different areas of drug development, such as clinical

development, pharmacovigilance and Medical Affairs.

ThromboGenics has recently relocated all of the Company's Belgian based staff into new, more spacious facilities at the 'Bioincubator' park in Leuven, Belgium. The move to this facility, which contains both laboratories and offices, is







designed to further strengthen the ThromboGenics culture and to enhance the linkage between the Company's scientists, development team and senior management.

ThromboGenics global outlook is reflected in its activities in 2008 to search out new cutting edge science and projects to drive its R&D pipeline. Throughout the year,

the Company has extended its network of academic and potential corporate partners in Europe, North America and Asia.

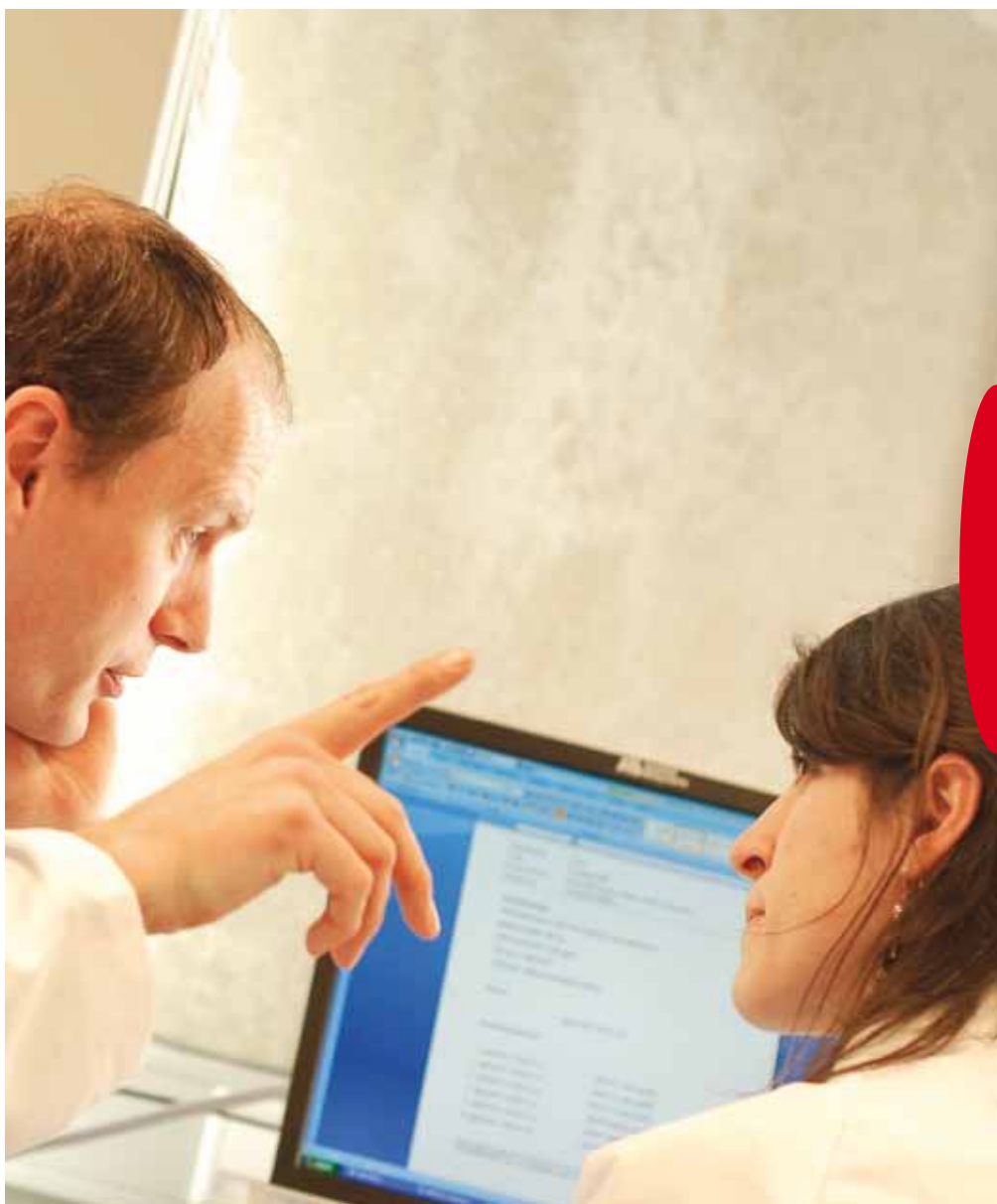
These potential new partners will build on the Company's well-established academic collaborations with KULeuven, Flanders Institute for Biotechnology (VIB), and Life Science Research Partners (LSRP). These collaborations, as well as the Company Scientific Advisory boards, enable the Company to develop its early stage pipeline and demonstrate the strong scientific heritage that has been a key factor in ThromboGenics' success.

In parallel with its search for new product opportunities, ThromboGenics is continuing to focus on building an internationally competitive, efficient and flexible organization, which has the capabilities to maximize the



potential of its current product portfolio, as well as further novel projects as they arise. Key to achieving this target is the ability of the Company to recruit additional talented people with different career backgrounds from all over the world, and allow them to flourish in an optimal organizational structure. To support these activities, the Human Resources team has continued to work on a number of internal and external programs that are designed to reinforce the Company's scientific and academic foundations.

2009 promises to be an exciting year for ThromboGenics as it continues to develop its clinical programs and move its research forward. The Company is confident it is equipped with the necessary skills, passion and culture to ensure that it can continue to generate further value from its development pipeline and organization.



## The Board of Directors



From left to right above: Staf van Reet, Luc Philips, Chris Buyse, Patrik De Haes  
Sitting: Désiré Collen, Jean-Luc Dehaene | Missing: Landon Clay

**“ The ThromboGenics board of directors is composed of experienced people from different disciplines and with a broad view on the Life Sciences industry. ”**

The ThromboGenics board of directors is composed of experienced people from different disciplines and with a broad view on the Life Sciences industry.

The executive members are Professor Désiré Collen, Chairman and founder of ThromboGenics, and Chris Buyse, CFO.

At an Extraordinary General Meeting held on April 9, 2009, Patrik De Haes was appointed as a director of ThromboGenics.

The non-executive members are board members who are not employed by the Company. They are the following: Landon T. Clay, Manager Member of East Hill Advisors, LLCC and partner of East Hill University Spinout Funds; Jean-Luc Dehaene, former prime minister of Belgium and vice-chairman of the European Convention; Luc Philips, Chairman of KBC Insurances and director of Kredietbank NV; Staf van Reet, Chairman of Movetis.

## The Management Team

The management team is composed of 8 members all having considerable experience in research, clinical development, commercialization

and financing of pharmaceutical compounds; **Patrik De Haes**, Chief Executive Officer, **Chris Buyse**, Chief Financial Officer, **Stuart Laermer**, Chief Business Officer, **Steve Pakola**, Chief Medical Officer, **Jean Marie**

**Stassen**, Head of Pre-Clinical Development, **Phil Challis**, Head of Chemistry, Manufacturing and Controls, **Andy De Deene**, Head of Program Management and **Laurence Raemdonck**, Head of Human Resources.



From left to right: Andy De Deene, Jean Marie Stassen, Patrik De Haes, Chris Buyse, Laurence Raemdonck, Phil Challis



Stuart Laermer, Steve Pakola

The members of the management team also make up the Executive Committee which convenes on a regular basis to discuss the Company's internal operations, and enables each member to be up-to-date on what is happening within the organization.

**Patrik De Haes**

Chief Executive Officer

**Patrik De Haes** has over 20 years of experience in the global health care industry, covering product development, marketing and general management. He joined from Roche in Switzerland, where



he was Head of the Global Insulin Infusion business. Before that, Patrik was President and CEO of Disetronic Medical Systems Inc, a leading company in insulin infusion therapy, in Minneapolis, USA. At Sandoz Pharma (now Novartis) in Switzerland, he led the global development and commercialization of the first biotech product for that company. Patrik holds a degree in Medicine from the University of Leuven.

### Chris Buyse

Chief Financial Officer

**Chris Buyse** brings to ThromboGenics 20 years experience in international company finance and in running and establishing best financial practice. He was previously CFO of the Belgian biotechnology company CropDesign, where he coordinated its acquisition by BASF in early 2007. Before this, Chris was Finance Director of WorldCom/MCI Belux, a European subsidiary of one of the world's largest telecom companies, and

was CFO and interim CEO of Keyware Technologies, reporting to the Chairman of the Board. In addition, he held several financial positions as financial controller and internal auditor at Spector Photo Group, Suez Lyonnaise des Eaux and Unilever. Chris holds a Master Degree in Economics from the University of Antwerp and an MBA from the Vlerick Management School in Gent.

### Stuart Laermer

Chief Business Officer

**Stuart Laermer** is responsible for the Company's commercial activities, including partnering, licensing and business development. Stuart has more than 20 years of global experience in the commercialization of novel technologies. He was formerly Vice President, Business Development at Synthon Chiragenics and Physiome Sciences, where he was a member of the founding management team. He has also been Director, Business Development at Hoffmann-La

Roche and Director, Biotechnology & Specialty Products at Fisher Scientific. Stuart received his MSc in Chemical Engineering from Columbia University, and MBA from New York University.

### Steve Pakola

Chief Medical Officer

**Steve Pakola** is a licensed physician with extensive clinical trial experience, including over 11 years in pharma/biotech clinical development. Prior to joining the Company, Steve was Associate Director, Cardiovascular Clinical Research, at Boehringer-Ingelheim Pharmaceuticals, where he served as global medical lead on the lipid-lowering development program, as well as U.S. medical lead for the direct thrombin inhibitor development program. Prior to Boehringer-Ingelheim, he also served in senior-level clinical development positions at Quintiles Cardiovascular Therapeutics and Organon, Inc. Steve received his MD degree from the University of Pennsylvania.

**Jean Marie Stassen**

Head of Pre-Clinical Development

**Jean Marie Stassen** is responsible for ThromboGenics' preclinical program capability.

Jean-Marie joined ThromboGenics in 2001 and is co-founder and member of the board of FlandersBio. He was previously at Boehringer Ingelheim Pharma, Germany, where he served as a research project leader for the cardiovascular therapeutic area. As a preclinical expert, he was deeply involved in the European registration of the thrombolytic TNKase™ (Tenecteplase). Together with Désiré Collen, Jean-Marie worked on the characterization of tPA and staphylokinase. He is author and co-author of more than 100 papers in peer-reviewed journals, and more than 250 patents and patent applications.

**Phil Challis**

Head of Chemistry,  
Manufacturing and Controls

**Phil Challis** brings over 20 years of experience in product

development of biological entities. Phil has previously worked for UCB Pharma in a management role, and brings ThromboGenics experience in defining manufacturing strategy. He has managed manufacturing programs during early and late phase clinical trials and post commercialization. Phil has previously held key positions in product development functions at Lonza Biologics and Celltech, and brings valuable experience to ThromboGenics' strategic manufacturing policy.

**Andy De Deene**

Head of Program Management

**Andy De Deene** previously worked as both Manager and Director for both the Janssen Research Foundation and XCellentis in Belgium and has considerable experience in different areas of drug development such as clinical development, pharmacovigilance and Medical Affairs. Andy holds a MD from the University of Ghent, was trained as a dermatologist

at the University of Cologne, and obtained an executive MBA at the Vlerick Management School.

**Laurence Raemdonck**

Head of Human Resources

**Laurence Raemdonck** joined ThromboGenics as HR Manager in 2007. She has a Masters Degree in Germanic Philology as well as a degree in Human Resources. Laurence was previously employed in the telecom sector at Verizon Business. She has the responsibility for all areas related to human resources, such as compensation, hiring, performance management, benefits, organization development, administration and training. As HR Manager, she is advocate for both the Company and its people, and therefore performs a constant balancing act in order to meet both needs successfully.



# ThromboGenics

ThromboGenics

Financial information

2008



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# Annual report 2008

## Language of this annual report

ThromboGenics published its Annual Report in Dutch. ThromboGenics has also produced an English translation of this Annual Report. In the event of differences of interpretation between the English and the Dutch versions of the Report, the original Dutch version has priority.

## Availability of the annual report

The Annual Report is available free of charge for the public upon request to:

**ThromboGenics NV**

to the attention of Chris BUYSE

Gaston Geenslaan 1

3001 Leuven

Tel. 016/75 13 10

Fax 016/75 13 11

e-mail: [chris.buyse@thrombogenics.com](mailto:chris.buyse@thrombogenics.com)

For information purposes only, there is also an electronic version of the Annual Report which can be obtained via the internet from the ThromboGenics website ([www.thrombogenics.com](http://www.thrombogenics.com)). Only the printed Annual Report is legally valid.

## Future-oriented information

This Annual Report includes future-oriented statements, expectations and assessments with regard to the expected future performances of ThromboGenics and the market in which it operates. Certain of these statements, expectations and assessments can be recognized by the use of words such as, but not limited to, “believe”, “anticipate”, “expect”, “intend”, “plan”, “strive”, “estimate”, “could”, “will” and “continue” and comparable expressions. They include all matters which are not historical fact. Such statements, expectations and assessments are based on various assumptions and assessments of known and unknown risks, uncertainties and other factors which were deemed to be reasonable when they were made, but which may or may not prove to be correct. Actual events are difficult to predict and can depend on factors outside the Company’s control. Consequently, it is possible that the actual results, financial condition, the results of the sector, will diverge substantially from any future results, performances or achievements expressed or implied by such statements, expectations and assessments. Factors which can cause such a divergence include, but are not limited to, the factors which are discussed in the Chapter “Risk Factors”. Given these uncertainties, absolutely no statement is made with regard to the correctness or reasonableness of such future-oriented statements, expectations and assessments. Moreover, they apply only on the date of this Annual Report. The Company expressly declines any obligation to adapt any of the future-oriented statements, expectations and assessments in this Annual Report in order to reflect change in the expectations of the Company in that respect, or any change in the facts, conditions or circumstances on which such statements, expectations and assessments are based, except to the extent that this is required by Belgian law.

All statements and information relate to the period up to 31 December 2008, unless expressly stated otherwise.

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## **Risks associated with the activities of ThromboGenics**

### **Development of a new drug takes a long time before it reaches the market**

The Group must conduct extensive pre-clinical and clinical trials of its drug candidates in order to demonstrate their safety and efficacy in humans before it can receive the necessary approval from the regulatory authorities to market these drug candidates. Clinical trials are expensive and time-consuming, and their results are highly uncertain.

The Group cannot guarantee that the drug candidates will demonstrate sufficient safety or efficacy in the studies to obtain marketing approval. Moreover, the results from earlier pre-clinical or clinical trials may not accurately predict the results of later-stage trials. The clinical trials may be suspended or terminated if participating subjects are exposed to unacceptable health risks, or if the drug candidates cause undesired side effects. Clinical trials may be discontinued or the development of the drug candidates may be abandoned if the clinical trials produce negative or inconclusive results.

### **Government regulation**

The products of ThromboGenics must receive marketing approval from the European Agency for the Evaluation of Medicinal Products (EMA), from the US Food and Drug Administration (FDA) or from regulatory authorities in other jurisdictions before the drug candidates may be marketed in a specific market. Each regulatory authority can impose its own requirements and can refuse to give the approval or can ask for additional data before giving the marketing approval for the product, even if such approval was already given by other authorities. Changes in the policy of the regulatory authorities for granting approval or the introduction of additional requirements by the regulatory authority for granting approval can mean that drug candidates do not get marketing approval at all, or at any rate that such approval is delayed. Moreover, the process for obtaining approval from the regulatory authorities is expensive and highly time-consuming, and the period necessary for obtaining the marketing approval is difficult to predict.

### **Dependency on partners**

The Group relies on third-party clinical investigators to conduct its clinical trials and other third parties to oversee the operations of such clinical trials, to perform data collection and analysis, safety reporting and other activities. The Group may have no or limited control over these third parties and the Group cannot guarantee that they will perform their obligations in an efficient and timely manner. If the clinical investigators and other third parties fail to meet their obligations, the Company may experience significant delays or failures in its clinical development programs and in the commercialization of its drug candidates.

Enrolling patients in the studies depends on many factors, including :

- the limited number of patients available for clinical trials, due to (e.g.) competition for patients by clinical trial programs for other treatments;
- the therapeutic endpoints chosen for evaluation;
- the eligibility criteria for the clinical trial;
- the size of the patient population required for analysis of the trial's therapeutic endpoints;
- the Group's or its potential future partners' ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the proportion of patients leaving the study before reaching an endpoint; and
- the availability of adequate insurance.

The Company or its potential future partners may experience difficulties in enrolling patients in clinical trials, which could increase the costs of these trials and adversely affect their timing and outcome.

**ThromboGenics may be unable to in-license or purchase new drug candidates on commercially attractive terms.**

The Company relies on its ability to develop promising new intellectual property and compounds with a high commercial potential via Flanders Interuniversity Institute for Biotechnology (VIB) and KULeuven and other partners or via its own internal research and development. ThromboGenics intends either to license the rights to such compounds, to purchase them or to acquire companies which own them. As a result, its future success partly depends on its ability to establish collaborations with third parties to license promising new compounds or to finance the licensing or purchase of these compounds or the companies that own them.

**The Company relies on third parties to supply the active pharmaceutical ingredients for some of its drug candidates.**

The Company relies on third parties to supply the active pharmaceutical ingredients of its drug candidates and to manufacture clinical and commercial quantities of them. If ThromboGenics loses any of these third parties as partners and/or Contract Manufacturing Organizations (CMOs) or they fail to provide ingredients of a satisfactory quality, in sufficient quantities, at acceptable prices and in a timely manner, the clinical development and commercialization of its drug candidates could be materially delayed.

**Reliance on collaborative partners**

The Company is dependent on current and future collaborative arrangements with experienced partners to complete the development of its existing and future drug candidates and to commercialize them successfully. These collaborative arrangements may place the development and commercialization of its drug candidates outside of the Group's control and may require the Company to relinquish important rights. If the Group fails to enter into collaborations on favorable terms or at all, its ability to develop and commercialize its existing or future drug candidates could be delayed and its costs of development and commercialization could increase.

**The Group's dependence on collaborative arrangements with experienced partners subjects it to a number of risks, including the following:**

- the Company may not be able to control the amount or timing of resources that its collaborative partners devote to its drug candidates;
- the Company may be required to relinquish important rights, including intellectual property, marketing and distribution rights;
- the Company may not receive any future milestone payments or royalties if a collaborator fails to develop or commercialize one of its drug candidates ;
- a collaborator may develop a competing drug candidate either by itself or in collaboration with others.
- the willingness or ability of a collaborator of the Company to fulfill its obligations under the collaboration arrangements may be adversely affected by changes in the collaborator's business strategy;

If any of these risks were to materialize, the Company's ability to develop and commercialize one or more of its drug candidates could be impaired.

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### **No background of operational profitability**

Upon commercialization, the Group's drug candidates may not gain acceptance by patients, physicians and other healthcare professionals. Market acceptance of the Group's drug candidates will depend on, among other things, the Group's ability to demonstrate the drug candidates' clinical efficacy, safety, cost-effectiveness, convenience and ease of administration as well as its other advantages over alternate treatments. Additionally, the Company's or its partners' ability to promote and market its drug candidates and its ability to obtain sufficient coverage or reimbursement from third party payers may impact the commercial success of its drug candidates. If the Group's drug candidates fail to gain market acceptance, it may have a material adverse impact on the Group's ability to generate revenues.

### **The pharmaceutical market is highly competitive**

The market for pharmaceutical drugs is highly competitive. The Company faces significant competition in the research, licensing, development and commercialization of its drug candidates.

The Group's competitors may bring drugs to the market more rapidly than the Company and may develop drugs which are more effective, more affordable or with better side effect profiles than the Company's drugs and drug candidates. Competing drugs may gain faster or greater market acceptance than the Company's drugs and medical advances or rapid technological development by competitors may result in the Company's drug candidates becoming non-competitive or obsolete before the Company is able to recover its research and development and commercialization expenses.

### **Patents and property rights**

The Group's success will depend in part on the ability of the Group and its licensees to obtain, maintain and enforce its patents and other intellectual property rights. The Company's drug candidates are covered by several patent families, which are either licensed to the Group or owned by the Group. The Group cannot guarantee that it or its licensors will be able to obtain or maintain these patents rights against third-party challenges to their validity, scope and enforceability.

Because patent law in the biopharmaceutical industry is highly uncertain, the Group cannot assure that its current or future patent applications will be issued. Nor can the Company assure that the scope of its current or future patents will be sufficiently broad to provide commercially meaningful protection against infringement by third parties.

The Group also relies on trade secrets and proprietary know-how to protect its drugs, drug candidates and production platforms. The Group makes reasonable efforts to maintain its trade secrets, but it cannot assure that its partners, employees, consultants, advisors or other third parties will not willfully or unintentionally disclose proprietary information to competitors.

The enforcement of patents, trade secrets, know-how and other intellectual property is costly, time-consuming and highly uncertain. The Group cannot guarantee that it will be successful in preventing the misappropriation of its patents, trade secrets, know-how and other intellectual property rights and those of its licensors.

### **The Group may infringe on the patents or intellectual property rights of others and may face patent litigation, which may be costly and time-consuming.**

The Group's success will depend in part on its ability to operate without infringing on or misappropriating the proprietary rights of others. The Group cannot guarantee that its activities, or those of its licensors, will not infringe on the patents owned by others. The Group may expend significant time and effort and may incur substantial costs in litigation if the Company is required to defend against patent suits brought against the Group or its licensors. If the Group or its licensors are found to infringe on the patents or other intellectual property rights of others, it may



be subject to substantial claims for damages, which could materially impact the Company's cash flow and financial position.

**Dependence on and ability to attract key personnel and managers.**

Being a small company with approximately 45 employees and managers, the Group's success depends on the continued contributions of its principal management and scientific personnel and on its ability to develop and maintain important relationships with leading academic institutions, scientists and companies in the face of intense competition for such personnel, institutions and companies. Although ThromboGenics generally has not experienced substantial problems retaining key employees, its employees can terminate their employment with the Group at any time.

**The Group has for most of its history incurred operating losses**

In 2008 Thrombogenics made its first net profit due the upfront payment it received from Roche in relation to its licensing of TB-403. However prior to this ThromboGenics Ltd, which was, incorporated in 1998, has incurred net losses on a consolidated level every year. The Group anticipates that in future it may make further net losses as it incurs additional research and development and general and administrative expenses in its efforts to further develop and commercialize its drugs and drug candidates. These losses, among other things, will cause the Group's working capital and shareholders' equity to decrease. If the Company is unable to successfully develop and commercialize its drugs and drug candidates, the Company may never become profitable on a consistent basis.

**Need for additional financing and access to capital**

The Group is confident that its current cash position will be sufficient to carry out the business plan as it now stands for at least the next 2 years. The Company's future financing needs will depend on many factors, including the progress, costs and timing of its research and development activities, the costs and timing of obtaining regulatory approval, the costs of obtaining, maintaining and enforcing its patents and other intellectual property rights, the costs and timing of maintaining or obtaining manufacturing for its drugs and drug candidates, the costs and timing of establishing sales and marketing capabilities and the terms and timing of establishing collaborations, licence agreements and other partnerships.

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# I. General information and information concerning the responsibility for the annual brochure and for the audit of the annual accounts

## I.1. Responsibility for the contents of this document

ThromboGenics' board of directors is responsible for the contents of this document. ThromboGenics declares that, having taken all reasonable care to ensure that such is the case, the information contained in this year's report is, to the best of its knowledge, in accordance with the facts and contains no omission likely to affect it materially.

## I.2. Responsibility for the audit of the annual accounts

KPMG Bedrijfsrevisoren, a company incorporated under Belgian law, having its registered office at Bourgetlaan 40, B-1130 Brussels, represented by Michel Lange and member of the "Instituut der Bedrijfsrevisoren (IBR)" has been appointed as statutory auditor of ThromboGenics for a term of three years ending immediately after the closing of the annual shareholders' meeting to be held in 2010 that will have deliberated and resolved on the financial statements for the financial year ending on 31 December 2009.

## 2. Key figures

### 2.1. Consolidated balance sheet

In '000 Euro – According to IFRS

	2008	2007
<b>ASSETS</b>		
Property plant and equipment	1,004	1,057
Intangible Assets	2,092	
Goodwill	2,586	2,586
<b>Fixed Assets:</b>	<b>5,682</b>	<b>3,643</b>
Trade and other receivables	2,527	1,533
Investments	28,565	6,710
Cash and cash equivalents	30,356	40,111
<b>Current Assets</b>	<b>61,448</b>	<b>48,354</b>
Pension	73	39
<b>Long-term Assets</b>	<b>73</b>	<b>39</b>
<b>Total Assets</b>	<b>67,203</b>	<b>52,036</b>
<b>EQUITY AND LIABILITIES</b>		
Share capital	111,338	110,309
Share premium	15,837	15,647
Accumulated translation differences	28	9
Other reserves	(20,851)	(21,476)
Retained earnings	(43,959)	(56,054)
<b>Equity attributable to equity holders of the parent</b>	<b>62,393</b>	<b>48,435</b>
<b>Minority interests</b>		
<b>Total Equity</b>	<b>62,393</b>	<b>48,435</b>
Trade payables	3,865	3,085
Other short-term payables	945	516
Short-term liabilities	4,810	3,601
<b>Total Equity and Liabilities</b>	<b>67,203</b>	<b>52,036</b>

## 2.2. Consolidated income statement

In '000 Euro, except per share amounts - According to IFRS

	Full year 12 months	Full year 12 months
	2008	2007
<b>Revenues</b>	<b>30,421</b>	<b>1,503</b>
<b>OPERATING RESULT</b>	<b>10,587</b>	<b>(17,417)</b>
Finance income	3,348	1,780
Finance expenses	(1,750)	(321)
<b>Result before income tax</b>	<b>12,185</b>	<b>(15,958)</b>
Income tax expenses	(90)	(9)
<b>Net result for the period</b>	<b>12,095</b>	<b>(15,967)</b>
<b>Earnings per share</b>		
Basic earnings per share	0.47	(0.67)
Diluted earnings per share	0.45	(0.62)

## 3. Activities of ThromboGenics

### 3.1. General

ThromboGenics NV was incorporated on 30 May 2006 and is a limited liability company (in Dutch: naamloze vennootschap). The registered office is established at

Gaston Geenslaan 1  
3001 Leuven  
Belgium  
Tel: +32 (0)16 75 13 10  
Fax: +32 (0)16 75 13 11

The company is registered in the Crossroads Databank for Enterprises under enterprise number 0881.620.924.

### 3.2. Mission

ThromboGenics develops innovative biopharmaceuticals, according to the strictest scientific and ethical standards, in order to create sustainable value for each of its stakeholders.

ThromboGenics develops drugs for a number of important therapeutic areas including back of the eye disease, vascular disease and cancer. The company has applied its in-house expertise to building up an important portfolio of promising drug candidates, most of which are already in the clinical phase.

### 3.3. History

Thromb-X was the original company of the Group. It was founded by Prof. Collen and the KULeuven in 1991 to develop new thrombolytics with better efficiency, less side effects and lower production costs by using the experience of Prof. Collen gained during the development of the successful thrombolytic drug tPA.

In 1992, Thromb-X moved to an up to-date research center next to the Center for Molecular and Vascular Biology of the KULeuven. In 1995, the Center for Transgene Technology and Gene therapy of the VIB moved into in the same building. Through close cooperation with the KULeuven and the VIB, the Company was able to move certain promising research programs through development.

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The initial R&D efforts of Thromb-X aimed at the development of staphylokinase, a promising thrombolytic for acute myocardial infarction. Because of strategic and commercial reasons, the Company decided to progress this development outside the Western market. In the mean time, Thromb-X successfully developed microplasmin, a recombinant derivative of the plasmin protein, in cooperation with the KULeuven and the VIB. This became the main focus of the Company. During this period, the Company expanded its preclinical and clinical development programs into indications outside the cardiovascular market. In 1998, ThromboGenics Ltd – an Irish company based in Dublin – became part of the company structure to speed up the clinical development of the Company's programs. In 1998, Biggar Ltd acquired 5,000,000 shares of ThromboGenics Ltd at a rate of IR € 1.00 per share and thereby became the biggest shareholder of ThromboGenics Ltd.

In 2001, East Hill Biopharmaceutical Partners invested about USD 12.8 million (about EUR 14.6 million) in ThromboGenics Ltd. At that time, Thromb-X became a subsidiary of the Irish company. With the growth of the Company, it became clear that more access to US expertise was needed in the areas of clinical development and business development. Therefore, in 2003, ThromboGenics Ltd acquired a subsidiary ThromboGenics Inc. based in New York.

In May 2006, ThromboGenics NV, a Belgian company with headquarters in Leuven, was incorporated as holding company of ThromboGenics Ltd, Thromb-X NV and ThromboGenics Inc.

The Company was able to finance its development through both equity financing and royalties from the tPA. tPA which was licensed to Genentech achieved at its peak annual sales of over USD 500 million. The license agreement with Genentech generated total royalties of USD 144 million, of which the Company received USD 51 million. The Company has 3 research collaboration agreements, with BioInvent International AB (Sweden), with Geymonat SpA (Italy) and with NuVue Technologies Ltd (USA).

## 3.4. Activities

The activities of ThromboGenics are focused on the development of new pharmaceuticals. At present there are 5 clinical programs and 2 pre-clinical programs running.

### 3.4.1. Clinical programs

- **Microplasmin for the treatment of back of the eye diseases**

ThromboGenics is developing microplasmin as a potential non-surgical treatment for focal vitreomacular adhesion. Focal vitreomacular adhesion is a condition in which the vitreous gel, in the center of the eye, has an abnormally strong adhesion to the retina at the back of the eye. This adhesion can cause vessel and retinal distortion which results in deterioration in the patient's vision. Moreover, vitreomacular adhesion is thought to play a key role in numerous back of the eye conditions such as macular hole formation, and some forms of macular edema. Vitreomacular adhesion is also associated with a much poorer prognosis in certain major eye indications including diabetic retinopathy and exudative Age-related Macular Degeneration (AMD).

Today the only treatment available for vitreomacular adhesion is vitrectomy. Vitrectomy is a surgical procedure which involves the removal of the vitreous from the eye using suction.

Microplasmin is a proteolytic enzyme which should simplify, and in some cases even replace, vitrectomy. It can induce 'posterior vitreous detachment' by breaking down the protein structures which hold together the vitreous and the retina. As a result, microplasmin has the potential to become a well-tolerated, efficacious treatment which has less risks and lower costs than vitrectomy.



The Phase III clinical program with microplasmin for the non-surgical treatment of back of the eye diseases began in January 2009. The program involves two clinical trials, taking place in the United States (TG-MV-006 trial) and Europe and the United States (TG-MV-007 trial). Both trials are multi-centre, randomized, placebo controlled, double-masked trials which will evaluate 125µg of microplasmin versus placebo in the intravitreal treatment of patients with focal vitreomacular adhesion. The trials will enroll approximately 320 patients each across approximately 40 centers in the United States (TG-MV-006) and 40 centers in Europe and North America (TG-MV-007).

- **Microplasmin for the treatment of cardiovascular diseases**

The primary objective in the treatment of thrombotic diseases is to unblock the blood vessels as quickly as possible. Most anti-thrombotic agents do not function optimally because it takes too long for the blood clot to dissolve, and moreover they can cause significant side effects, such as hemorrhages.

Microplasmin works directly on the blood clots whereas other anti-thrombotic agents activate plasminogen. This means that most other anti-thrombotic agents need to have the presence of plasminogen in the blood clots and the blood before they can exert their activity and therefore their effect depends on a number of factors. The direct action of microplasmin in thrombotic disease can be of importance above all with older blood clots, where the plasminogen content of the clot has declined significantly.

At the end of 2008 ThromboGenics announced positive results from the MITI IV (Microplasmin in Treatment of Ischemic stroke - IntraVenous) Phase II study that evaluated the safety and efficiency of microplasmin when administered intravenously to patients with acute stroke.

The study found that microplasmin was generally well tolerated. In addition, the study provided some interesting preliminary efficacy results.

After reporting these promising results from the Phase II trials with microplasmin, ThromboGenics has decided that it will only move forward with the development of microplasmin for vascular indications in cooperation with a partner, given the costs and risks involved.

- **Staphylokinase**

Staphylokinase is also an anti-thrombotic drug. Phase II studies in which microplasmin was used for the treatment of heart attacks have been successfully concluded. It was demonstrated that the activity of staphylokinase is comparable to that of tPA, one of the most widely-used thrombolytics for the treatment of heart attacks. However, the cost of staphylokinase is much lower than that of tPA. This can mean a major expansion in the standard treatment of heart attacks.

ThromboGenics has concluded licence agreements with Bharat Biotech (India) and with Rhein Minapharm (Egypt) for the production, further clinical development and commercialization of two forms of staphylokinase, THR-100 and THR-174. From both agreements, double-figure royalties will be generated from the sales of each drug.

- **TB-402 (anti-factor VIII)**

ThromboGenics is developing TB-402, an anti-Factor VIII antibody that binds with Factor VIII, an essential blood clotting factor, and thus influences the blood clotting mechanism. TB-402 is being developed as an anti-clotting agent with long-term action for the treatment of deep vein thrombosis and atrial fibrillation. The development of TB-402 is being done as part of the Company's joint venture with BioInvent (Sweden),

A Phase I clinical study has demonstrated the safety and tolerability of TB-402.

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TB-402 is a recombinant human monoclonal antibody that targets Factor VIII, a key component of the coagulation cascade. TB-402 is a novel anticoagulant agent, which may deliver important clinical benefits due to it only partially inhibiting Factor VIII activity even when given in very high doses. This novel mode of action is expected to reduce the risk of undesirable bleeding events and the need for patient monitoring, the two main drawbacks associated with current anticoagulants. In addition, TB-402 is a long-acting agent which means that patients are expected to receive just one single dose after surgery to prevent the development of DVT, as opposed to all current treatment options which require daily treatment for up to several weeks.

A Phase II trial with TB-402 started in February 2009 with the enrolment of the first patients. The study is an active (enoxaparin)-controlled, dose-escalating, multicenter, prospective, randomized, open label trial evaluating TB-402 for the prophylaxis of DVT after knee surgery. The study will assess three different doses of TB-402 given as a single intravenous bolus injection post knee replacement surgery. The trial will enroll 300 patients across 36 centers mainly in Central Europe. The primary endpoint is the safety and efficacy of the three escalating doses of TB-402. It is anticipated that the study will conclude by the end of 2010.

- **TB-403 (anti-PlGF)**

In June 2008 ThromboGenics and BioInvent announced a strategic alliance with Roche for TB-403, their jointly developed novel anti-cancer antibody. TB-403 is an innovative monoclonal antibody that inhibits placental growth factor (PlGF), a growth factor that is responsible for the formation of blood vessels. TB-403 (anti-PlGF) has the potential to be a breakthrough in the treatment of cancer. It is a humanized monoclonal antibody that blocks the formation of the new blood vessels required by solid tumors to support growth. Clinical evidence suggests that it plays a role in the angiogenesis of malignant tissue, and does not affect normal tissue angiogenesis.

Under the terms of this agreement, ThromboGenics and BioInvent received an initial upfront payment of 50 million Euro, with the potential of milestone payments of up to 450 million Euro following completion of a series of development and commercial milestones, as well as double digit royalties on future sales, included the sales of back-up antibodies that inhibit PlGF. ThromboGenics, that discovered TB-403, receives 60% and BioInvent 40% of the revenue from the deal. Roche will obtain a global license to develop and commercialize TB-403. ThromboGenics and BioInvent will be entitled to the co-promotion rights for this product in the Benelux, the Baltic states and in Northern Europe.

The first Phase I clinical study with TB-403 (anti-PlGF) has been completed. Recently the approval to start a Phase Ib study with escalating doses was received. This Phase Ib study in patients with advanced cancer is ongoing in Denmark.

TB-403 is a humanized monoclonal anti-PlGF (placental growth factor) antibody that blocks the formation of new blood vessels in solid tumors. By blocking the formation of new blood vessels (anti-angiogenesis), TB-403 has the potential to reduce the growth and spread of cancer cells.

### **3.4.2. Pre-clinical programs**

- **Anti-VPAC**

In collaboration with the Catholic University of Leuven, ThromboGenics is investigating whether the inhibition of VPAC stimulates the production of blood platelets. VPAC is a receptor on the surface area of the bone marrow cells which are responsible for the production of blood platelets. The accelerated production of blood platelets is important for combating thrombocytopenia, a side effect of chemotherapy in the treatment of cancer. The current treatment by transfusion of blood platelets is a risky and only temporary solution. Pre-clinical trials show how the inhibition of VPAC promotes the production of adult bone marrow cells, which can accelerate the formation of blood platelets.

In February 2009 ThromboGenics announced that it had been awarded a 3.2 million Euro grant for the development of its anti-VPAC1 antibody for cancer chemotherapy induced thrombocytopenia.

The grant represents an important source of funding to support the development of this novel product which is expected to begin clinical trials in 2011. The grant has come from the Institute for the promotion of Innovation by Science and Technology in Flanders (IWT) and is based on the successful completion of a series of development milestones over the next three years. IWT is a public institution which was created by the Flemish government to provide R&D and innovation support to projects based in Flanders.

- **PLGF**

The use of PLGF is exclusively licensed from the Flanders Interuniversity Institute for Biotechnology (VIB) and ThromboGenics is developing PLGF under a collaboration agreement with Geymonat (Italy). PLGF is produced by recombinant DNA technology.

PLGF is a naturally-occurring protein that stimulates the formation of blood vessels. The indications which could benefit from treatment with PLGF are coronary artery diseases and Peripheral Arterial Occlusion, where PLGF can stimulate blood vessel formation. This may enable it to counter the effects of tissue which is dying off or helping to repair damaged tissue. Pre-clinical trials demonstrate that PLGF could produce a large number of new and complete functional blood vessels.

## 3.5. Intellectual Property

**The Company's drug candidates are covered by several patent families that are either owned by the Company or exclusively licensed to the Company.**

The licenses awarded to ThromboGenics NV are exclusive licenses with the right to sublicense. The (sub)licenses awarded from ThromboGenics NV to ThromboGenics Ltd are exclusive (sub)licenses. By the merger of these two companies ThromboGenics NV will have the rights to all in-house intellectual property. The Company employs an internal IP counsel who works in collaboration with several leading international patent law firms.

## 3.6. Group structure

As of 31 December 2008 ThromboGenics has two subsidiaries, ThromboGenics Ltd based in Dublin (Ireland), a company under Irish law with registered office at the Arthur Cox Building, Earlsfort Terrace 2, Dublin, and ThromboGenics Inc., a company under American law with registered office at 1560 Broadway, 10th Floor, New York, NY 10036, USA.

On February 20, 2009 both Board of Directors of ThromboGenics NV and Board of Directors of ThromboGenics Ltd approved a merger proposal between the two entities. This proposal will be submitted for approval on the first general shareholders meeting.

## 3.7. Facilities

Since January 2009 all of the Company's labs have been located at the "Bio-Incubator" building at the Gaston Geenslaan 1 at 3001 Leuven. ThromboGenics entered into a lease agreement for this building with Bio-Incubator NV for a period of 5 years starting July 1, 2008.

Currently the Company occupies a number of state-of-the-art research laboratories, including cell culture rooms, a molecular biology laboratory, an analytical laboratory, a prokaryotic fermentation suite, a purification suite, and all the

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necessary support and storage rooms. The Company has access to 1250 square meter state-of-the-art laboratories and offices.

The Company produces research-grade products and reagents in production laboratories of approximately 250 square meters.

ThromboGenics is in the process of implementing the ISO 17025 standard. The Company adheres to GLP-GMP for stability testing and has obtained GLP status for drug formulation analysis and toxicological studies.

### 3.8. Investment policy

Apart from investments in lab materials and hardware and software, ThromboGenics has not made any other large investments, nor made commitments to make major investments in the near future. With regard to the move of the company's labs in early 2009, the labs were modernized and the company made some new improvements. R&D investments will be directly financed and as such they are not considered as investments that are capitalized on the balance sheet according to accounting rules, applied by the IFRS, only costs made for the start of the Phase III MIVI Trust study are capitalized in the company's balance sheet.

### 3.9. Health, safety and environmental regulations

As a biotech company, ThromboGenics has to deal with biological waste on a daily basis. The health and safety of personnel and visitors and environmental protection constitute a priority for the company. The environmental, health and safety policy is a key element of the Company's business strategy and is included in the objectives of each employee.

ThromboGenics' is focused on creating a safe environment, not only for the Company's employees, but also for visitors and the overall environment.

### 3.10. Recent trends

The company expects an increase in research and development costs in 2009. This is partly attributable to an increase in staff costs, but mainly to an increase in the costs for clinical studies, primarily due to the start of the Phase III MIVI Trust study.

The prospects for 2009 will also depend on whether or not specific agreements are concluded with existing or new partners.

# 4. Corporate Governance

## 4.1. General provisions

This section summarizes the rules and principles by which the corporate governance of ThromboGenics is organized. It is based on the articles of association and on the corporate governance charter of the Company which was drawn up on 19 October 2006 and updated on 19 December 2007.

ThromboGenics' board of directors intends to comply with the Belgian Corporate Governance Code, but believes that certain deviations from its provisions are justified in view of the company's particular situation. These deviations are further explained below.

Due to the size of the Company, the board of directors combined the nomination committee and the remuneration committee and has not set up a management committee in accordance with article 524bis of the Belgian Company Code.

At the time of its incorporation, the Company appointed Prof. D. Collen as its chairman and CEO, thus departing from the principle of article 1.5 of the Belgian Corporate Governance Code.

On September 1, 2008 Prof. D. Collen stepped down as CEO of ThromboGenics. However, Prof. Collen remains as the Chairman of the board of directors of ThromboGenics. Prof. Collen was succeeded by Dr. Patrik De Haes as the Company's CEO.

ThromboGenics' Corporate Governance Charter contains the following specific chapters:

- General Information
- Board of Directors
- Audit Committees
- Nomination and Remuneration Committee
- CEO

The charter is available on the company's website ([www.thrombogenics.com](http://www.thrombogenics.com)) under Investors Relations/Corporate Governance and can be obtained free of charge via the company's registered office. In this reference document we present an abridged version of the charter.

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#### **4.1.1. Composition of the board of directors**

The board of directors currently consists of six members. These members are listed in table 1. The board of directors regards Dr. Van Reet, Mr. L. Philips and Mr. J.L. Dehaene as independent directors: The following paragraphs contain a brief biography of each director:

##### **Désiré Collen (Patcobel NV), Voorzitter, Chairman, executive director**

Prof. Collen holds an MD degree (1968) and a PhD degree in Chemistry (1974) from the University of Leuven (Belgium) and until 2008, was director of the Center for Transgene Technology and Gene Therapy of the Flanders Interuniversity Institute for Biotechnology (V.I.B) in Leuven, Belgium.

Until October 2007 he was also director of the Centre for Molecular and Vascular Biology and chairman of the Molecular and Cellular Medicine Department of the KULeuven.

He specializes in the molecular biology of hemostasis and thrombosis, the development of new thrombolytic and anti-thrombotic agents, the pathogenesis and treatment of atherosclerosis, and gene targeting and gene transfer studies of the cardiovascular system. He has received four honorary doctorates (Erasmus Universiteit, Rotterdam, Netherlands; Vrije Universiteit Brussel, Brussels, Belgium; University of Notre Dame, IN, US; Université de la Méditerranée, Marseille, France), and several scientific awards, including the Francqui Prize (Belgium) in 1984, the Prix Louis Jeantet de Médecine (Switzerland) in 1986, the Bristol-Myers-Squibb Award for Cardiovascular Research (US) in 1995, and the Interbrew-Baillet Latour Health Prize in 2005. Mr. Collen has co-authored more than 650 scientific publications, and is co-inventor of over 20 issued patents and patent applications. His team discovered and developed tPA, currently the most effective drug for thrombolysis and as treatment for acute myocardial infarction (heart attack).

##### **Chris Buyse (Sofia BVBA), executive director**

Mr. Chris Buyse (44) brings to ThromboGenics 20 years of international financial expertise and experience in introducing best financial management practices. He was CFO of the Belgian biotech company CropDesign, where in July 2006 he coordinated the acquisition by BASF. Before that Mr. Buyse was financial manager of WorldCom/MCI Belux, a European subsidiary of one of the world's largest telecommunication companies, and was CFO and interim CEO of Keyware Technologies, reporting to the chairman of the board of directors. In addition, he also held several financial positions as financial controller and internal auditor at Spector Photo Group, Suez Lyonnaise des Eaux and Unilever. Chris Buyse is holding a master degree in applied economic sciences at the University of Antwerp and he is holder of an MBA from the Vlerick Management School in Gent.

##### **Landon T. Clay, non-executive director**

Mr. Clay is a Managing Member of East Hill Advisors, LLC and general partner of East Hill University Spinout Funds. Before he co-founded East Hill, he was chairman and Chief Executive Officer (CEO) of Eaton Vance Corporation, an investment management company listed on the NYSE. He is chairman of the Clay Mathematics Institute, which he founded in 1998, ADE Corporation and the Caribbean Conservation Corporation and is also director of Golden Queen Mining Co. Ltd. He was a member of the board of directors of the Museum of Fine Arts, Boston, Middlesex School and the Smithsonian Institute, Washington DC. Mr. Clay received an AB, cum laude, from Harvard College and served as an Overseer of Harvard from 1975 to 1981. He taught mathematics and scientific archaeology at Harvard and financed Harvard's share in the construction of the Magellan Telescope in Chile.

##### **Jean-Luc Dehaene, non-executive, independent director**

Mr. Dehaene has occupied several ministerial posts. He was Prime Minister of Belgium from 1992 to 1999 and vice-chairman of the European Convention. He is a member of the board of directors of Umicore NV, InBev NV and



Lotus Bakeries NV. In October 2008 he was appointed chairman of Dexia NV/SA. He is also chairman of the board of directors of the College of Europe (Bruges) and vice-president of the Koning Boudewijnstichting. He is a member of the European Parliament. Mr. Dehaene studied law and political and economic sciences in Namur and Leuven, Belgium.

#### **Luc Philips (Lugost BVBA), non-executive, independent director**

Luc Philips holds a degree in Commercial and Financial Sciences and is Chairman of the Board of Directors of KBC Verzekeringen.

In 1997 he was appointed as a member of the Board of Directors and the Management Committee of Kredietbank N.V. From 1998 to 2003 he was Managing Director of KBC Bankverzekeringsholding and KBC Bank. He was appointed as Managing Director of Almanij in 2003. In that same year he was also appointed as a Director of KBC Bankverzekeringsholding, KBC Bank, KBC Verzekeringen and KBL and he became chairman of the Audit Committee KBC Bankverzekeringsholding, KBC Bank and KBC Verzekeringen. After the merger of KBC Bankverzekeringsholding with Almanij, Luc Philips remained chairman of the Audit Committee of KBC Group and KBC Bank, he became a member of the Audit Committee KBC Verzekeringen and he became Chairman of the Board of Directors of KBC Verzekeringen and Director of KBC Bank and KBC Group. In addition, he sits on several Boards of Directors of companies which form part of KBC Group NV, 3 of which are active in Central Europe (K & H Bank in Hungary and Kredyt Bank and TuiR Warta in Poland). On May 1, 2009 he will take up the responsibilities of the CFRO of KBC Group. Luc Philips is also a member of the Board of Directors of Norkom Technologies (Ireland) and the Gemma Frisius Fonds (Belgium).

#### **Staf Van Reet (Viziphar Biosciences BVBA), non-executive, independent director**

Dr. Van Reet is chairman of Movetis NV and managing director of Viziphar Biosciences BVBA, a start-up bio-pharma research and development company, and its subsidiary Viziphar Biosciences PVT Ltd (Bangalore, India), of which he is also chairman of the board of directors. He also is a director at the Flanders Interuniversity Institute for Biotechnology (VIB) and of Okapi Sciences NV. Dr. Van Reet was formerly active at Johnson & Johnson, a.o. as a member of the Group Operating Committee of the pharmaceutical division; he was managing director of Janssen Pharmaceutica NV and Janssen Biotech NV and chairman of the Janssen Research Foundation. From 2000 until 2004 Dr. Van Reet was vice president of Johnson & Johnson Development Corporation, the venturing arm of Johnson & Johnson, and from April until June 2005 he was a member of the management committee of Galapagos NV. Mr. Van Reet holds a degree of engineering in Applied Biological Sciences and a PhD in Agricultural Sciences from the University of Leuven (Belgium) and studied law at the University of Antwerp (Belgium). He is a qualified Belgian and European Patent Authority.

At an Extraordinary General Meeting held on April 9, Dr. P. De Haes was appointed as a director of ThromboGenics.

#### **Litigation statement concerning directors**

On the date of this Annual Report, none of the directors of the Company or, in the event of companies which act as director, none of their permanent representatives, has for at least the previous five years:

- had any convictions in relation to fraudulent offences;
- held an executive function in the form of a senior manager or a member of the administrative, management or supervisory bodies of any company at the time of or preceding any bankruptcy, receivership or liquidation; or been subject to any official public incrimination and/or sanction by any public or regulatory authority (including any designated professional body); or
- ever been disqualified by a court from acting as a member of the administrative, management or supervisory bodies of a company or from acting in the management or conduct of the affairs of any company.

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## 4.2. Board of Directors' meetings in the financial year 2008

During the financial year 2008, the board of directors held 4 meetings. Apart from specific items, the Board is primarily focused on the progress of the company across all operational activities: business development, clinical trials, CMC and production, human resources and finances.

## 4.3. Committees within the board of directors

The board of directors has established an audit committee and a combined nomination and remuneration committee. The board of directors appoints the members and the chairman of each committee. Each committee consists of at least three members. The composition of the committee over the financial year 2008 was as follows:

- Audit Committee: Mr. Luc Philips (Lugost BVBA), chairman, Dr. Staf Van Reet (Viziphar Biosciences BVBA) and Mr. Jean-Luc Dehaene.

The Audit Committee held 2 meetings during the financial year.

- Nomination and Remuneration Committee: Dr. Staf Van Reet (Viziphar Biosciences BVBA), chairman, Mr. Landon Clay and Mr. Jean-Luc Dehaene.

The Nomination and Remuneration Committee held 2 meetings during the financial year.

The powers of these committees are described in ThromboGenics' Corporate Governance Charter (sections 3 and 4), which is available on the ThromboGenics website ([www.thrombogenics.com](http://www.thrombogenics.com)).

## 4.4. Conflicts of interest of directors and transactions with affiliated companies

### 4.4.1. Conflicts of interest of directors

Article 523 of the Belgian Company Code contains special provisions which must be complied with whenever a director has a direct or indirect conflicting interest of a patrimonial nature in a decision or transaction within the authority of the board of directors.

According to article 523, §1 of the Belgian Company Code, the director having a direct or indirect conflicting interest of a patrimonial nature shall notify the other directors thereof prior to a decision of the board of directors relating to such conflicting interest. His/her statement and the grounds justifying the aforementioned conflict of interest must be recorded in the minutes of the board of directors' meeting at which such decision is taken.

With a view to its publication in the annual report, the board of directors must describe in the minutes the nature of the contemplated decision or the transaction and shall account for the decision taken. The minutes shall also mention the patrimonial consequences thereof for ThromboGenics. The annual report must contain the aforementioned minutes in their entirety.

The director concerned shall also inform the auditor of his/her conflicting interest. The (annual) report of the statutory auditors must contain a separate description of the patrimonial consequences for ThromboGenics of the decisions of the board of directors in respect of which there is a conflicting interest.

The director concerned also may not participate in the deliberations or voting of the board of directors on such decisions or transactions in respect of which there is a conflicting interest.

At this moment the directors have no conflict of interest as understood in article 523 of the Belgian Company Code that was not notified to the board of directors.

Art. 524bis of the Company Code provides for a similar procedure in the event of conflicts of interest for members of the management committee. If such a conflict develops, only the Board of Directors is competent to take the decision which gave rise to the conflict of interest. The executive management is not a management committee as understood in article 524bis of the Company Code.

#### 4.4.2. Transactions with affiliated companies

Article 524 of the Belgian Company Code provides for a special procedure which must be followed for transactions with ThromboGenics' affiliated companies or subsidiaries. Such a procedure does not apply to decisions or transactions that are entered into in the ordinary course of business at usual market conditions or for decisions and transactions whose value does not exceed 1 percent of ThromboGenics' consolidated net assets.

### 4.5. Transactions with related parties

1. In September 2006, ThromboGenics NV signed a rental agreement with Life Sciences Research Partners VZW (LSRP). This rental agreement was ended by mutual consent during the course of 2008 as a result of which the agreement formally ended on 31 December 2008.

Over the account year 2008 a total of 59,325 Euro was charged as a rental fee. In the last 2 trimesters 75% of the rental cost was charged.

2. In May 2007 ThromboGenics decided to outlicense the antibodies against blood platelets-glycoprotein Ib (anti-GPIb) and von Willebrand factor (anti-vWF) to LSRP VZW for an amount of 1,100,000 Euro and 25% share in any future income that LSRP might receive for this program.
3. With regard to research, ThromboGenics has patent, license and collaboration agreements with certain shareholders such as Désiré Collen and third parties such as the VIB (Flanders Interuniversity institute for Biotechnology). In 2008, 4,500,000 Euro were paid to the VIB within the framework of the F. Hoffmann La Roche AG agreement. The VIB shares 50% of this income with LSRP.
4. Désiré Collen, Chris Buyse and Patrik De Haes are compensated by means of a management agreement between ThromboGenics NV and respectively Patcobel NV (a company of which Désiré Collen is director), Sofia BVBA (a company of which Chris Buyse is director) and ViBio BVBA (company of which Patrik De Haes is director). Within the framework of these consulting agreements the ThromboGenics Group paid a total of 709,153 Euro in 2008, and 476,738 Euro was paid in 2007.
5. For non-executive directors a total of 79,000 Euro was charged in 2008 and 74,000 Euro in 2007, for the execution of their board mandate.

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## 4.6. Relations with significant shareholders

Désiré Collen is remunerated through (i) a management agreement between ThromboGenics NV and Patcobel NV (i.e. the company of which Désiré Collen is managing director) and (ii) an exclusive consultancy agreement between ThromboGenics Ltd and Patcobel NV.

## 4.7. Executive management

### (i) General provisions

The Board of Directors has appointed the CEO of the company. The powers of the CEO were defined by the Board of Directors in close consultation with the CEO.

The CEO supervises the various activities and the central services of the company. The CEO together with the CFO, CBO, CMO, Head of Pre-Clinical Development, Head of Chemistry, Head of Program Management and Head of HR constitute the executive management of ThromboGenics. The executive management does not constitute a management committee as understood in article 524bis of the Belgian Company Code.

### (ii) The executive management is composed of:

**Patrik De Haes, MD** – *Chief Executive Officer*

Dr. De Haes brings to ThromboGenics extensive experience in the pharmaceutical industry. Over the past 20 years he has held various positions in product development, marketing and general management at a number of major companies in the Life Science sector. Before he began working at ThromboGenics, Dr. De Haes was Senior Vice-President of Global Infusion Business of Roche Diagnostics, Bern, Switzerland and he was a member of the Executive Committee of Roche Diabetes Care. Prior to the acquisition by Roche, he was President and CEO of Disetronic Medical Systems Inc., Minneapolis, US, leader in insulin pump therapy, where he led its successful transformation into one of the most rapidly growing MedTech companies in the US. Dr. De Haes also held positions in drug development at Sandoz Pharma (now part of Novartis), where he was responsible for the development and commercialization of the very first biotech product of this company. Dr. De Haes received his MD degree from KULeuven, Belgium and he also holds a degree in Marketing Strategy from INSEAD, Fontainebleau, France. He also earned a corporate MBA, University of St. Thomas, Minneapolis, US.

**Chris Buyse** – *Chief Financial Officer*

Chris Buyse is CFO of the Company and as such has served on the board of directors since August 2006. Within the company he is responsible for the financial management, corporate communications and mergers & acquisitions. He has 20 years of international financial expertise and experience in introducing best financial management practices. He was CFO of the Belgian biotech company CropDesign where earlier this year he coordinated the acquisition by BASF. Before that, Mr. Buyse was financial manager of WorldCom/MCI Belux, a European subsidiary of one of the world's largest telecommunication companies, and was CFO and interim CEO of Keyware Technologies, reporting to the chairman of the board of directors. In addition, he also held several financial positions as financial controller and internal auditor at Spector Photo Group, Suez Lyonnaise des Eaux and Unilever. Chris Buyse is holding a master degree in applied economic sciences at the University of Antwerp and an MBA from the Vlerick Management School in Gent.

**Stuart Laermer MSc, MBA** – *Chief Business Officer*

Mr. Laermer is Chief Business Officer of ThromboGenics, responsible for the Company's commercial activities, including partnering, licensing and business development. Mr. Laermer brings to the company more than 20 years of global experience in the commercialization of novel technologies. He was formerly Vice President, Business Development at Synthon Chiragenics and Physiome Sciences, where he was a member of the founding management team, as well as Director, Biotechnology & Specialty Products at Fisher Scientific and Director, Business Development at Hoffmann-La Roche. At Synthon, Mr. Laermer launched that company's discovery program for the development of new drug classes targeted at anti-infective, autoimmune, cancer and diabetes. At Physiome Sciences, he directed the company's efforts at commercializing a computational platform for drug discovery, which allowed the creation of virtual cells, tissues and organs. At Fisher Scientific, Mr. Laermer was responsible for establishing and executing the strategy for Fisher's global biotechnology business, and actively leading new ventures in state-of-the-art technology platforms. At Roche, he was responsible for the launch of several new biotechnology ventures, including the commercialization of alpha interferon (Roferon®). Mr. Laermer has published in the field of polymer stabilization and holds patents in this area. He received his BSc in Chemistry from Brandeis University, MSc in Chemical Engineering from Columbia University, and MBA from New York University.

**Steve Pakola, MD** – *Chief Medical Officer*

Dr. Pakola, who joined the Company in May 2000, is Chief Medical Officer and also a member of the board of directors of ThromboGenics Ltd. Dr. Pakola is a licensed physician with extensive clinical trial experience, including 10 years in pharma/biotech clinical development (predominantly in the cardiovascular therapeutic area). Prior to joining the Company, Dr. Pakola was Associate Director, Cardiovascular Clinical Research, of Boehringer-Ingelheim Pharmaceuticals, where he served as global medical lead on the lipid-lowering development program, as well as US medical lead for the direct thrombin inhibitor development program. Prior to Boehringer-Ingelheim, Dr. Pakola also served in senior-level clinical development positions at Quintiles Cardiovascular Therapeutics and Organon, Inc. Dr. Pakola received his BS (summa cum laude with honors, Phi Beta Kappa) and his MD degree (with honors distinction) from the University of Pennsylvania.

**Jean Marie Stassen, PhD** – *Head of Pre-Clinical Development*

Dr. Stassen is Senior Director of Pre-Clinical Development and joined ThromboGenics in 2001. Dr. Stassen is co-founder and member of the board of FlandersBio. At Boehringer-Ingelheim Pharma, Germany, Dr. Stassen served as a research project leader for the cardiovascular therapeutic area, and as internal advisor concerning neurological diseases. As a pre-clinical expert, he was deeply involved in the European registration of Tenecteplase. At KULeuven, Dr. Stassen was involved in basic research at the Centre for Molecular and Vascular Biology, where he worked on anti-thrombotic and thrombolytic therapy. Together with Prof. Collen, Dr. Stassen worked on the characterization of tPA and staphylokinase. He is author and co-author of more than 90 papers in peer-reviewed journals, and more than 250 patents and patent applications. Dr. Stassen received his MD degree from the University of Umeå in Sweden.

**Phil Challis** – *Head of Chemistry, Manufacturing and Controls (CMC)*

Mr. Challis brings over 20 years of experience in product development of biological entities. Phil has previously worked for UCB Pharma in a management role and brings ThromboGenics experience in defining manufacturing strategy, planning late phase regulatory submissions. He has managed manufacturing program during early and late phase clinical trials and post commercialization. Phil has previously held key positions in product development functions at Lonza Biologics and Celltech and brings valuable experience to ThromboGenics.

**Andy De Deene** – *Head of Program Management*

Andy De Deene worked formerly as a director of the Jansen Research Foundation and of XCellentis in Belgium and has elaborate experience in the different areas of drug development, as well clinical development, pharmacovigilance and

medical affairs. Dr. De Deene studied medicine at the Rijksuniversiteit in Gent and at the University of Köln where he received a degree as dermatologist. He also graduated as a MBA at the Vlerick Management School.

#### **Laurence Raemdonck** – *Head of Human Resources*

In 2007 Laurence Raemdonck joined ThromboGenics as HR Manager. She is licensed in Germanic Philology and possesses a degree in Human Resources. She was previously employed in the telecom sector at Verizon Business. She has the responsibility for all areas related to human resources, such as compensation, hiring, performance management, benefits, organization development, administration and training. As HR Manager, she is advocate for both the company and the people who work in the company.

## **4.8. Employees including headcount development**

As of 31 December 2008, the Company employed 46 personnel and management, 37 in ThromboGenics NV (Leuven, Belgium), 4 in ThromboGenics Ltd (Dublin, Ireland) and 5 in ThromboGenics Inc. (New York, US).

Table: Headcount evolution as total number of staff at year-end including management.

	2003	2004	2005	2006	2007	2008
ThromboGenics NV (*) (Leuven, Belgium)	27	33	32	30	30	37
ThromboGenics Ltd (Dublin, Ireland)	6	5	6	5	6	4
ThromboGenics Inc. (New York, US)	3	3	4	5	5	5
<b>Total</b>	<b>36</b>	<b>41</b>	<b>42</b>	<b>40</b>	<b>41</b>	<b>46</b>

(\*) included Thromb-X, that January 1, 2007 merged with ThromboGenics NV

The Company expects that the total number of employees could rise to around 55 by the end of 2009. The personnel of the Company counts 14 personnel holding a doctoral degree and 16 personnel holding a master degree.

## **4.9. Remuneration of the Directors and executive management**

### **(a) Remuneration of the Directors**

The non-executive directors each receive an annual remuneration of EUR 10,000 and, in addition, the non-executive directors receive EUR 2,000 for each meeting of the board of directors, the audit committee or the nomination and remuneration committee which they attend.

Patcobel NV and Sofia BVBA will not receive a separate remuneration for their director's mandate.

The Board of Directors believes that the remuneration package is justified, because it is in line with the prevailing practices and expectations of smaller listed companies. Moreover, the company can thus offer an appropriate remuneration in order to attract experienced independent directors from different economic sectors.



There is no agreement between the company and the non-executive directors with regard to a compensation or indemnification as a result of the termination of their mandate.

## **(b) Remuneration of the executive management**

The remuneration of the executive management is determined by the Board of Directors on recommendation of the appointment and remuneration committee. The remuneration is designed to attract, retain and motivate executive managers.

The remuneration of the members of the executive management consists of the following elements:

- Each member of the executive management is entitled to a fixed basic remuneration which is adapted to the responsibilities, the relevant experience and the powers and which are in line with the market conditions for similar positions.
- Each member of the executive management also receives the possibility to participate in a warrant-based incentive program, in conformity with the recommendations of the appointment and remuneration committee.
- Moreover, each member of the executive management is entitled to a number of additional benefits in kind. In most cases this involves participation in hospitalization insurance, a mobile telephone, a laptop computer or other benefits depending on the general company policy or the local customs, which can differ between Belgium and the United States. For expatriates, housing costs can be defrayed on a temporary basis.

In early 2008, a variable element of remuneration was put in place for executive management. Payment of this variable element depends on the extent to which the executive management has achieved the Company's business objectives.

Some members of the executive management are employed on the basis of employment contracts. These agreements are usually of unlimited duration. The company can terminate these agreements subject to respecting a termination indemnity which conforms with local legal and social obligations.

Other members are employed on the basis of a service agreement. Members of the executive management who fulfill their assignment under a service agreement have no right to additional benefits, apart from them receiving a laptop computer which conforms with the general policy of the company.

The total consulting fee, included the costs for Patcobel NV, ViBio BVBA and Sofia BVBA amounts respectively to EUR 477 Keuro for 2007 and EUR 709 Keuro for 2008.

However, the composition of the management was modified during this two year period. Sofia BVBA started its mandate in August 2006 and ViBio BVBA started its mandate in February 2007. In September 2008 ViBio BVBA took over the responsibilities as a CEO from Patcobel NV.

On 31 December 2008 the executive management companies hold 281,000 warrants, of which 102,000 have already vested. The strike prices on these warrants vary from EUR 4,91 Euro to EUR 11.05.

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# 5. Shares and Shareholders

## 5.1. Share capital and shares

On 31 December 2008, the share capital of ThromboGenics NV amounted to EUR 115,801,804.48, represented by 25,730,789 shares, all with the same fractional value. Under section “Consolidated overview of modifications to equity” an overview is offered of the evolution of the company’s share capital since its incorporation on 30 May 2006.

The extraordinary shareholders’ meeting of the Company held on 7 June 2006 decided to increase ThromboGenics’ share capital by way of a Contribution in Kind of the shares in ThromboGenics Ltd on a share-for-share basis. In return for the contribution of one share in ThromboGenics Ltd a shareholder of ThromboGenics Ltd received one share in ThromboGenics NV. The shares in ThromboGenics Ltd were contributed at a value per share equal to the final Offer Price (IPO).

The same extraordinary general meeting decided to increase the share capital of the Company by EUR 35,000,001.

On 7 June 2006 the extraordinary shareholders’ meeting of ThromboGenics NV decided (i) to cancel the above-mentioned existing authorization of the board of directors concerning the share capital as granted in the deed of incorporation and (ii) to grant a new authorization to the board of directors to increase ThromboGenics NV’s share capital in one or more transactions by a maximum amount equal to ThromboGenics NV’s share capital as established at completion of the Offering.

If the capital is increased within the limits of the authorized capital, the board of directors will be authorized to request payment of an issue premium. If the board of directors so resolves, this issue premium will be booked on a non-available account, which may only be decreased or disposed of by a resolution of a shareholders’ meeting taken in accordance with the provisions governing an amendment of the articles of association.

This board of directors’ authorization will be valid for capital increases subscribed for in cash or in kind, or made by capitalization of reserves, with or without issuing new shares. The board of directors is authorized to issue convertible bonds or warrants within the limits of the authorized capital.

The board of directors is authorized, within the limits of the authorized capital, to restrict or exclude the pre-emption right of the shareholders in the interest of ThromboGenics and in accordance with article 596 and following of the Belgian Company Code. The board of directors is authorized to restrict or exclude the pre-emption right of the shareholders in favor of one or more persons, even if these persons are not members of the personnel of ThromboGenics or its subsidiaries.

## 5.2. Warrant plans

ThromboGenics has created a number of warrants. Paragraph 6.28 gives more detailed information on the warrant plans and outstanding warrants at the end of 2008.

## 5.3. Shareholders

The following table shows the Company's largest shareholders at the end of 2008 on the basis of the notifications which the company has received from parties who, by means of a transparency declaration, have informed the company of their ownership of ThromboGenics shares.

Name	Notification Date	Shares	% total number of shares
Landon Clay	01/10/2008	2,576,448	10.0
Biggar Ltd	01/10/2008	2,512,105	9.8
KBC Asset Management	01/10/2008	1,755,431	6.8
Petercam	01/10/2008	1,474,289	5.7
O.G.B.A van Herk BV	01/10/2008	1,119,940	4.3
The Clay Mathematics Institute	01/10/2008	1,099,247	4.3

## 5.4. Notification of important participations

Belgian law, in conjunction with ThromboGenics' articles of association, imposes disclosure requirements on any individual or entity acquiring or transferring voting securities or securities which give a right to voting securities, as soon as, following such acquisitions or transfer, the total number of voting rights directly or indirectly held by such individual or entity, alone or in concert with others, increases above or falls below a threshold of 3 percent, 5 percent, or any multiple of 5 percent, of the total number of voting rights attached to the Company's securities. A shareholder whose shareholding increases above or falls below any such thresholds must, each time, disclose this fact to the BFIC and to the company. The documents pursuant to which the transaction was effected must be submitted to the BFIC. When the participation of a shareholder reaches 20 percent, the notification must indicate in which strategy the acquisition or transfer concerned fits, as well as the number of securities acquired during a period of 12 months before the notification and in which manner such securities were acquired. Such notification is also required if an individual or an entity acquires or transfers control (either direct or indirect, either de jure or de facto) in a company that possesses 3 percent of the voting rights of the company.

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The company is required to publicly disclose any notifications received regarding increases or decreases in a shareholder's ownership of ThromboGenics' securities on the next business day, and must mention these notifications in the notes to its annual accounts. Euronext Brussels will publish details of the notifications.

## 5.5. Financial service

The financial service for the shares will be provided in Belgium by KBC Bank, free of charge for the shareholders.

Shareholders must themselves solicit information with regard to costs relating to financial services offered by other intermediaries.

# 6. Consolidated financial statements

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## 6.I. Financial information

### 6.1.1. Consolidated profit and loss account

In thousands of Euro (years ended on 31 December)

	Note	2008	2007
<b>Income</b>		<b>30,421</b>	<b>1,503</b>
License income	7	30,335	1,252
Other income	7	86	251
<b>Cost of sales</b>	8	<b>(2,747)</b>	<b>(168)</b>
<b>Gross profit</b>		<b>27,674</b>	<b>1,335</b>
Research and development expenses	9	(15,712)	(17,232)
General and administrative expenses	10	(3,031)	(2,315)
Selling expenses	11	(493)	(413)
Other operating income	12	2,149	1,208
<b>Operating result</b>		<b>10,587</b>	<b>(17,417)</b>
Financial income	13	3,348	1,780
Financial expenses	14	(1,750)	(321)
<b>Result before income tax</b>		<b>12,185</b>	<b>(15,958)</b>
Income tax	17	(90)	(9)
<b>Net result for the period</b>		<b>12,095</b>	<b>(15,967)</b>
Attributable to:			
Equity holders of the company		12,095	(15,967)
<b>Result per Share</b>			
Basic earnings per share (Euro)	18	0.47	(0.67)
Diluted earnings per share (Euro)	18	0.45	(0.62)



## 6.1.2. Consolidated balance sheet

In thousands of Euro (years ended on 31 December)

	Note	2008	2007
<b>ASSETS</b>			
Property, plant and equipment	19	1,004	1,057
Intangible assets	20	2,092	
Goodwill	21	2,586	2,586
<b>Fixed Assets</b>		<b>5,682</b>	<b>3,643</b>
Trade and other receivables	22	2,527	1,533
Investments	23	28,565	6,710
Cash and cash equivalents	24	30,356	40,111
<b>Current Assets</b>		<b>61,448</b>	<b>48,354</b>
Pensions	29	73	39
<b>Long-term Assets</b>		<b>73</b>	<b>39</b>
<b>Total Assets</b>		<b>67,203</b>	<b>52,036</b>
<b>EQUITY AND LIABILITIES</b>			
Share capital	27	111,338	110,309
Share premium	27	15,837	15,647
Accumulated translation differences		28	9
Other reserves	28	(20,851)	(21,476)
Retained earnings		(43,959)	(56,054)
<b>Equity attributable to equity holders of the parent company</b>		<b>62,393</b>	<b>48,435</b>
<b>Minority interests</b>			
<b>Total equity</b>		<b>62,393</b>	<b>48,435</b>
Trade payables		3,865	3,085
Other short-term liabilities	25	945	516
<b>Short-term liabilities</b>		<b>4,810</b>	<b>3,601</b>
<b>Total equity and liabilities</b>		<b>67,203</b>	<b>52,036</b>

### 6.1.3. Consolidated cash flow overview

In thousands of Euro (years ended 31 December)

	2008	2007
<b>OPERATING ACTIVITIES</b>		
(Loss) profit for the financial year	12,095	(15,967)
Financial expenses	1,750	321
Financial income	(3,348)	(1,780)
Depreciation on property, plant and equipment	429	337
Pension liabilities	(34)	(68)
Costs of share-based payments	702	862
<i>Cash flows before modification of the working capital</i>	11,594	(16,295)
(Increase)/decrease in trade and other receivables including tax receivables	(846)	(76)
Increase / (decrease) in short-term liabilities	1,209	1,574
Received / (paid) taxes		
<b>Net cash flow from operating activities</b>	<b>11,957</b>	<b>(14,797)</b>
<b>Investment activities</b>		
Retirement of fixed assets	50	1
Investments	(22,045)	(6,025)
Interest received and similar income	2,108	1,630
Acquisition of intangible assets	(2,193)	
Acquisition of property, plant and equipment	(426)	(866)
<b>Net cash flow (used for) / generated by investment activities</b>	<b>(22,506)</b>	<b>(5,260)</b>
<b>FINANCING ACTIVITIES</b>		
Income from share issues	1,249	28,251
Paid interests	(3)	
<b>Net cash flow (used for) / generated by financing activities</b>	<b>1,246</b>	<b>28,251</b>
<b>Net increase (decrease) in cash flow and cash equivalents</b>	<b>(9,303)</b>	<b>8,194</b>
<b>Cash and cash equivalents at the start of the year</b>	<b>40,111</b>	<b>32,043</b>
Effect of exchange rate modifications	(452)	(126)
<b>Cash and cash equivalents at the end of the year</b>	<b>30,356</b>	<b>40,111</b>

#### 6.1.4. Consolidated overview of modifications to equity

	Share capital	Share premium	Cumulative translation differences	Other reserves	Retained earnings	Attributable to shareholders of the parent company	Minority interests	Total
Balance sheet as at 1 January 2007	95,974	-	(2)	(20,607)	(40,087)	35,278		35,278
Net loss 2007					(15,967)	(15,967)		(15,967)
Exchange rate differences as a result of retranslation of foreign subsidiary			11			11		11
Capital increase	9,965	13,947				23,912		23,912
Costs capital increase	(772)					(772)		(772)
Conversion of warrants by ThromboGenics Ltd				5,036			5,036	5,036
Contribution in kind ThromboGenics Ltd shares	5,075	1,692		(6,767)		5,036	(5,036)	
Conversion of warrants by ThromboGenics NV	90	8				98		98
Costs of exercising warrants	(23)					(23)		(23)
Share-based payment				862		862		862
Balance sheet as at 31 Dec. 2007	110,309	15,647	9	(21,476)	(56,054)	48,435		48,435
Net Profit 2008					12,095	12,095		12,095
Exchange rate differences as a result of retranslation of foreign subsidiary			19			19		19
Conversion of warrants by ThromboGenics Ltd				893			893	893
Contribution in kind ThromboGenics Ltd shares	777	86		(863)		893	(893)	
Share-based payment				702		702		702
Conversion of warrants by ThromboGenics NV	252	104				356		356
Fair Value Adjustment Investments				(107)		(107)		(107)
Balance sheet as at 31 Dec. 2008	111,338	15,837	28	(20,851)	(43,959)	62,393		62,393

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## 6.2. Notes to the consolidated annual accounts

### 6.2.1. Reporting entity

ThromboGenics NV, a *naamloze vennootschap* (limited company) established under Belgian law with its registered office at Gaston Geenslaan 1, B-3001 Heverlee, and its subsidiaries (ThromboGenics Inc. and ThromboGenics Ltd) are a biopharmaceutical group with a privileged position in the development of drugs for conditions related to the circulatory system. The ThromboGenics NV Group (the 'Group') has built up a substantial range of drug candidates, a number of which are at the clinical study stage. The Group focuses on the development of new drugs for the treatment of cardiovascular diseases, eye diseases and cancer. The Group's research and development facilities are located in Belgium.

The consolidated financial statements of ThromboGenics NV for the year ending 31 December 2008 include ThromboGenics NV and its subsidiaries and constitute the ThromboGenics NV Group.

These consolidated financial statements were approved by the Board of Directors on 12 March 2009.

### 6.2.2. Application of new and revised Standards and Interpretations

#### Standards and Interpretations in force in the current period

In the current year the Group has applied the following new Standards and/or Interpretations:

**IFRIC 11 IFRS 2** *"Group and treasury share transactions"*

The application of this Standard and Interpretation has no significant influence on the different components of the balance sheet nor on the results of the Group and did not lead to any change in the valuation bases used.

In addition the following new Standards and/or Interpretations have come into effect which are not relevant for the Group and therefore have not been applied:

**IFRIC 12** *"Service concession arrangements"*

**IFRIC 14 IAS 19** *"The limit on a defined benefit asset, minimum funding requirements and their interaction"*

#### Early adoption of Standards and Interpretations

The group had decided not to early adopt any new Standard or Interpretations.

#### Advanced application of Standards and Interpretations

The Group has decided not to apply any Standards or Interpretations in advance.

#### Standards and Interpretations issued but not yet applicable

On the date on which these financial statements were approved, the following standards and interpretations had been issued but were not yet applicable in the European Union:

**IAS 1** *'Presentation of Financial Statements'*, revision of the presentation of financial statements (applicable for financial years beginning on or after 1 January 2009). This standard replaces IAS 1 *'Presentation of Financial Statements'* (revised in 2003) as amended in 2005.

Amendment of **IAS 27** '*Consolidated and separate Financial Statements*' (applicable for financial years beginning on or after 1 July 2009). This standard amends the current version of IAS 27 '*Consolidated and separate Financial Statements*' (revised in 2003).

**IFRS 3** '*Business combinations*' (applicable to business combinations when the acquisition date falls on or after the start date of the first financial year or after 1 July 2009).

**IFRS 8** '*Operating Segments*' (applicable for financial years beginning on or after 1 January 2009)

Amendment of **IAS 23** '*Borrowing costs*' (applicable for financial years beginning on or after 1 January 2009)

Amendment of **IFRS 2** '*Group share transactions and own shares purchased*' (effective from 1 January 2009)

Amendment to IFRS 2; '*Share-based payments - vesting conditions and cancellations*'; (applicable for financial years beginning on or after January 1, 2009)

Amendment of **IAS 32** '*Financial Instruments: Presentation*' and amendment of **IAS 1**, '*Presentation of financial statements*' – '*Puttable financial instruments and obligations arising on liquidation*' (effective from 1 January 2009).

Following Standards have been changed as a consequence of the yearly IASB amelioration project of which the contents was published in May 2008:

- **IFRS 5** (Amendment), '*Non-current assets held-for-sale and discontinued operations*' (and consequential amendment to **IFRS 1**, '*First-time adoption*') (effective from 1 July 2009).
- **IAS 16** (Amendment), '*Property, plant and equipment*' (and consequential amendment to **IAS 7**, '*Statement of cash flows*') (effective from 1 January 2009).
- **IAS 19** (Amendment), '*Employee benefits*' (effective from 1 January 2009).
- **IAS 20** (Amendment), '*Accounting for government grants and disclosure of government assistance*' (effective from 1 January 2009).
- **IAS 27** (Amendment), '*Consolidated and separate financial statements*' (effective from 1 January 2009).
- **IAS 28** (Amendment), '*Investments in associates*' (and consequential amendments to **IAS 32**, '*Financial Instruments: Presentation*', and **IFRS 7**, '*Financial instruments: Disclosures*') (effective from 1 January 2009).
- **IAS 29** (Amendment), '*Financial reporting in hyperinflationary economies*' (effective from 1 January 2009).
- **IAS 31** (Amendment), '*Interests in joint ventures*' (and consequential amendments to **IAS 32** and **IFRS 7** (effective from 1 January 2009).

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- **IAS 38** (Amendment), '*Intangible assets*' (effective from 1 January 2009).
  - **IAS 39** (Amendment), '*Financial instruments: Recognition and measurement*' (effective from 1 January 2009).
  - **IAS 40** (Amendment), '*Investment property*' (and consequential amendments to **IAS 16**) (effective from 1 January 2009).
  - **IAS 41** (Amendment), '*Agriculture*' (effective from 1 January 2009).
  - There are a number of minor amendments to **IFRS 7**, '*Financial information: Disclosures*', **IAS 8**, '*Financial instruments: Disclosures*', **IAS 8**, '*Accounting policies, changes in accounting estimates and errors*', **IAS 10**, '*Events after the Balance Sheet Date*', **IAS 18**, '*Revenue*' and **IAS 34**, '*Interim financial reporting*', which are part of the IASB's annual improvements project published in May 2008 (not addressed above).

**IFRIC 13** "*Customer loyalty programmes*" (applicable for financial years beginning on or after 1 July 2008).

**IFRIC 15**, "*Agreements for construction of real estates*" (applicable for financial years beginning on or after 1 January 2009).

**IFRIC 16**, "*Hedges of a net investment in a foreign operation*" (applicable for financial years beginning on or after 1 October 2008).

**IFRIC 17**, "*benefits of non-monetary assets to shareholders*" (applicable to the consolidated financial statements of 2010).

**IFRIC 18** "*Transfers of assets from customers*" (applicable to the consolidated financial statements of 2010).

The adapted version **IFRS 1**, First-time adoption of IFRSs (2009).

The Board considers that the Standards and Interpretations are not relevant or that its application in future periods will have no significant impact on the financial statements of the Group during the period of initial application.



### 6.2.3. Basis of preparation and significant accounting policies up the financial statements

The main bases adopted when preparing these consolidated financial statements are set out below.

#### (a) Statement of compliance

These consolidated financial statements were prepared in accordance with the “*International Financial Reporting Standards*” (IFRS) as issued by the “*International Accounting Standards Board*” (IASB) and adopted by the European Union (hereinafter referred to as “IFRS”). The consolidated financial statements are presented in Euro.

#### (b) Basis of measurement

The financial statements were prepared on the basis of the historic cost price method, apart from certain items for which IFRS requires a different valuation principle. This deviation from the historic cost price method is declared in the summary of the main accounting principles. The accounting principles below were applied consistently for all periods presented in these accounts and for all group entities.

#### (c) Continuity

The consolidated financial statements were prepared on the assumption of continuity in the Group.

#### (d) Basis of consolidation

##### Subsidiaries

The consolidated financial statements include all the subsidiaries that are controlled by the Group. Control exists when ThromboGenics NV has the power, directly or indirectly, to govern the financial and business policies and obtains benefits from the entities' activities. Control is presumed to exist when ThromboGenics NV owns, directly or indirectly, more than 50 per cent of the voting rights linked to the share capital. The existence and effect of potential voting rights that are currently exercisable or convertible are considered when assessing whether the Group controls another entity.

Subsidiaries are fully consolidated from the date on which control is transferred to the Group. They are de-consolidated from the date on which control ceases.

Intra-group transactions, balances and unrealized profits and losses on transactions between companies in the group are eliminated when the consolidated financial statements are drawn up. Unrealized losses are eliminated in the same way as unrealized profits unless the transaction indicates an impairment loss on the assets transferred. The accounting principles of the subsidiaries have been adjusted where necessary to be consistent with the principles adopted by the Group.

##### Business combinations and goodwill

Business combinations are processed by applying the purchase method. The cost of a purchase is calculated on the basis of the fair value of the assets disposed of, the equity instruments disbursed as compensation and the obligations entered into or taken over on the date of the purchase, plus the costs directly attributable to the purchase. The cost is attributed to the identifiable assets, liabilities and contingent liabilities of the party taken over. These identifiable acquired assets and (contingent) liabilities are initially valued at their fair value on the date of purchase.

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The amount by which the cost of the purchase exceeds the fair value of the Group's interest in the identifiable acquired net assets is included in goodwill. If the purchase cost is lower than the fair value of the net assets of the subsidiary taken over, the remaining difference is included directly in the income statement after revaluation.

Goodwill is initially recognized as an asset at cost price and is then valued at cost price less the accumulated impairment.

#### **Changes in ownership interest of a subsidiary without losing control**

Subsequent increases in ownership interests in a subsidiary without losing control are transactions between shareholders of the entity as a whole, hence management considers them to be equity transactions. The carrying amount of the subsidiary's assets and liabilities is not affected and no additional goodwill is recognized. Any premium or discount is recognized directly in equity.

Minority interests in the net assets of consolidated subsidiaries are identified separately from the Group's equity. Minority interests consist of the amount of those interests at the date of the original business combination and the minority's share of changes in equity since the date of the combination. Losses applicable to the minority in excess of the minority's interest in the subsidiary's equity are allocated against the interests of the Group.

#### **(e) Foreign currency translation**

##### **Functional and presentation currency**

The consolidated financial statements are presented in thousands of Euro, which is the functional and presentation currency of ThromboGenics NV. All companies within the Group use the Euro as their functional currency, except for the US subsidiary, whose functional currency is the US dollar.

##### **Transactions and balances in foreign currencies**

Transactions in currencies other than the functional currency of the entities are recorded at the exchange rates prevailing on the date of the transaction. At each balance sheet date, monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing on the balance sheet date. Exchange rate differences relating to monetary items include the difference between the amortized costs in the functional currency at the start of the period, adjusted for the actual interest (payments) during the period, and the amortized costs of foreign currencies translated at the exchange rate at the end of the period. Non-monetary assets and liabilities carried at fair value that are denominated in foreign currencies are translated at the exchange rates prevailing on the date when the fair value was determined. Gains and losses arising on retranslation are included in the net profit or loss for the period, except for exchange differences arising on non-monetary assets and liabilities at fair value where the fluctuations in fair value are recognized directly in equity.

## Foreign operations

On consolidation, the assets and liabilities including goodwill and fair value adjustments arising on consolidation of the Group's foreign operations are translated at the exchange rates prevailing on the balance sheet date. Income and expense items are translated at the average exchange rates for the period. Exchange differences arising, if any, are classified as equity and transferred to the Group's translation reserve. Such translation differences are recognized as income or expense items in the period in which the operation is disposed of.

### (f) Revenue recognition

- Collected payments from research milestones are considered as revenue when these payments have been acquired. The sale agreement does not provide for reimbursement, and there should also be no fees.
- Royalties are generated under license agreements based on licensee sales of products incorporating the Group's proprietary technology. Royalties are recognized once the amounts due can be reliably estimated based on the sale of the underlying products and when collectability is assured. When the Group is unable to reliably estimate the royalty income due until receipt of the payment, the royalty income is accounted for as received rather than when due.
- Income from sales of products and license is recognized when all the following conditions have been met:
  - The significant risks and rewards of the ownership of goods have been transferred to the buyer;
  - The Group retains neither effective control nor involvement to the degree usually associated with ownership over the goods sold;
  - The amount of revenue can be measured reliably;
  - It is probable that the economic benefits associated with the transaction will flow to the entity; and
  - The costs incurred or to be incurred in respect of the transaction can be measured reliably.

### (g) Research grants

On certain specific research projects, the research costs incurred are partially reimbursed by IWT (Institute for the Promotion of Innovation in Science and Technology in Flanders – *Instituut voor de Aanmoediging van Innovatie door Wetenschap en Technologie in Vlaanderen* – 'IWT') or the European Union ('EU'). These grants are recognized as government grant income over the term of the grant project when there is a reasonable assurance the Group will comply with the conditions attached to them and the grants will be received. Grants that compensate the company for expenses incurred are recognized as other income in the income statement on a systematic basis in the same period in which the expenses are incurred.

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## **(h) Cooperation agreements for research and development**

The Group has entered into certain cooperation arrangements whereby the parties agree to work jointly on research into and development of potential therapeutic products. Under such arrangements the parties agree who will be performing which elements of the research and development projects. These arrangements do not include the creation of any separate entity to conduct the activities nor any separate and distinct assets or liabilities. The parties agree that the combined cost of all relevant activities will be borne by the parties in a particular proportion and that net revenues derived from sales of any resulting product will be shared in a particular proportion. The sharing of costs will result in balancing payments between the parties and such payments receivable or payable will be respectively added to or deducted from research and development expense in the income statement. Any amounts receivable or payable at a period end are included in the balance sheet under trade and other receivables or other current liabilities.

## **(i) Intangible assets**

### **1. Internally generated intangible assets**

Research costs are charged to the income statement as incurred.

An internally generated intangible fixed asset (see Point 2.20) that arises from development activities undertaken in the Group is recognized only if all of the following conditions are met:

- Technical possibility of making the intangible asset ready for use
- The intention is to complete the intangible asset and use or sell it
- Possibility of using or selling the intangible asset
- It is probable that the intangible asset will generate future economic benefit or demonstrate the existence of a market
- Availability of adequate technical, sufficient financial resources to complete the development
- Availability to reliably measure the attributed expenses for this intangible asset during development

The patent costs for protecting the intangible assets are recognized as an expense.

ThromboGenics activated in 2008 clinical study costs on microplasmin vitreoretinal due to the fact that this project is in phase III and future commercialization is estimated to be highly probable.

The initial amount of intangible assets consists of external study and production expenses from subcontracting on all projects entered into phase III. After their initial recording on the balance sheet intangible assets are valued at cost less accumulated depreciation and accumulated impairment losses. Depreciation of capitalized development costs are recognized in the income statement under research and development costs.

The capitalized costs are amortized over the life of the patent as of the moment that it will generate revenue.

Intangible assets are reviewed annually in case of special events to determine whether there is any indication of impairment. This is to assess whether there are indications that the assets are subjected to impairments. If such indications exist, the recoverable amount of the asset will be estimated to calculate the impairment.

In case the criteria for capitalization of the research and development expenses are not met, these expenses are recorded as incurred during the period.

## **2. Intangible assets purchased**

Computer software licenses acquired are capitalised on the basis of the costs incurred to acquire and bring to use the specific software. These costs are amortized over their estimated useful life which is normally considered to be three years.

Knowledge acquired in the form of licenses is recorded at cost less accumulated amortization and impairment. They are amortized on a straight line basis over their estimated useful life, which is the period over which the Group expects to receive economic benefits from such licenses.

## **3. Goodwill**

(Negative) goodwill arises from acquisition of subsidiaries, non-consolidated companies and joint ventures.

### Acquisitions before January 1, 2003

As part of the transition to IFRSs, the group elected to restate only those business combinations that occurred on or after January 1, 2003. In respect of acquisitions prior to 1 January 2003, goodwill represents the amount recognized under the Group's previous accounting framework, Irish GAAP.

### Acquisitions on or after January 1, 2003

For acquisitions on or after January 1, 2003, goodwill represents the excess of the costs of the acquisition over the Group's interest in the net fair value of the identifiable assets, liabilities and contingent liabilities of the acquiree. When the excess is negative (negative goodwill), it is recognised immediately in profit or loss.

Goodwill is measured at cost less accumulated impairment losses.

Goodwill results from the acquisition of Thromb-X by ThromboGenics Ltd in 2001.

## **(j) Property, plant and equipment**

Property, plant and equipment are included at the historical cost (material costs only) less accumulated depreciation and impairment. Subsequent costs are included in the carrying amount for the asset or booked as a separate asset as appropriate, but only when it is probable that future economic benefits associated with the item will be generated for the Group and the cost price of the item can be measured reliably. All other repair and maintenance costs are charged to the income statement as incurred. The cost of assets retired or otherwise disposed of and the related accumulated depreciation are included in the income statement as part of the gain or loss on disposal in the year of disposal. Gains and losses on disposal of property, plant and equipment are included in other income or expense.

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Depreciation is calculated using the straight-line method to allocate the cost of property, plant and equipment to their estimated residual values over their estimated useful lives as follows:

Buildings	25 years
Plant and equipment	3 to 5 years
Furniture and fittings	3 to 5 years
Leasehold improvements	over the term of the lease

The depreciation and amortization methods, useful life and residual value are re-valued on each reporting date.

#### Subsequent costs

The cost of replacing part of an item of property, plant and equipment is recognised in the carrying amount of the item if it is probable that the future economic benefits embodied within the part will flow to the Group and its cost can be measured reliably. The carrying amount of the replaced part is derecognised. The costs of the day-to-day servicing of property, plant and equipment are recognised in profit or loss as incurred.

#### **(k) Leased assets**

Leases are classified as finance leases whenever the terms of the lease transfer substantially all the risks and rewards of ownership to the lessee. All other leases are classified as operating leases.

Rentals payable under operating leases are included in the income statement on a straight-line basis over the relevant lease term.

#### **(l) Impairment losses on goodwill, intangible fixed assets and property, plant and equipment**

Intangible assets with an indefinite useful life or not yet available for use and goodwill are not subject to amortization but are tested annually for impairment.

Assets that are subject to amortization or depreciation are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. An impairment loss is recognized for the amount by which the carrying amount of the asset exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs to sell and its value in use. To determine its value in use, the cash value of the estimated future cash flows is calculated on the basis of a discount rate before tax that reflects both the current market appraisal of the time value of cash and the specific risks relating to the assets. For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). The impairment loss is allocated first to reduce the carrying amount of any goodwill allocated to the cash-generating unit pro rata the carrying amount of each asset in the unit. An impairment loss recognized for goodwill is not reversed in a subsequent period. For assets other than goodwill, where an impairment loss is subsequently reversed, the carrying amount of the asset (cash-generating unit) is increased to the revised estimate of its recoverable value, but so that the increased carrying amount does not exceed the carrying amount that would have been determined had no impairment loss been included for the asset (cash-generating unit) in prior years. The reversal of an impairment loss is included immediately in the income statement.

**(m) Income taxes**

Income tax expenses in the income statement comprise the tax currently payable and deferred tax.

The tax currently payable is based on taxable profit for the year. Taxable profit differs from net profit as reported in the income statement because it excludes items of income or expense that are taxable or deductible in other years and it further excludes items that are never taxable or deductible. The Group's liability for current tax is calculated using tax rates that have been enacted or substantively enacted on the balance sheet date.

Deferred tax is the tax expected to be payable or recoverable on differences between the carrying amounts of assets and liabilities in the financial statements and the corresponding tax bases used in the computation of taxable profit, and is accounted for using the balance sheet method.

Deferred tax liabilities are generally recognized for all taxable temporary differences and deferred tax assets are recognized to the extent that it is probable that taxable profits will be available against which deductible temporary differences can be utilized. Such assets and liabilities are not recognized if the temporary difference arises from goodwill (or negative goodwill) or from the initial recognition (other than in a business combination) of other assets and liabilities in a transaction that affects neither the tax profit nor the accounting profit.

Deferred tax liabilities are recognized for taxable temporary differences arising on investments in subsidiaries and associates, and interests in joint ventures, except where the Group is able to control the reversal of the temporary difference and it is probable that the temporary difference will not reverse in the foreseeable future.

The carrying amount of deferred tax assets is reviewed at each balance sheet date and reduced to the extent that it is no longer probable that sufficient taxable profits will be available to allow all or part of the asset to be recovered.

Deferred tax is calculated at the tax rates that are expected to apply in the period when the liability is settled or the asset realized. Deferred tax is charged or credited in the income statement, except when it relates to items charged or credited directly to equity, in which case the deferred tax is also dealt with in equity.

Deferred tax assets and liabilities are offset when they relate to income taxes levied by the same taxation authority and the Group intends to settle its current tax assets and liabilities on a net basis.



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## **(n) Employee benefit plan**

### **Pension obligations**

The Group operates one defined benefit plan, the assets of which are held in separate trustee-administered funds. A defined contribution plan is a plan for benefits payable after leaving the company whereby an entity transfers fixed contributions to a separate entity and has no legally enforceable or actual obligation to make further contributions. Obligations relating to contributions to pension schemes on the basis of defined contributions are included in the profit and loss account as an employee benefit expense when the amounts are payable. Prepaid amounts are included as assets insofar as a reimbursement in cash or a reduction in future payments is available.

The Group's commitments under defined benefit plans, and the related costs, are valued using the "projected unit credit method" with actuarial valuations being carried out at each balance sheet date by a qualified actuary. Actuarial gains and losses that exceed 10 per cent of the greater of either the present value of the Group's defined benefit obligation or the fair value of plan assets are amortized over a period equal to the expected average remaining working lives of the participating employees. Past service cost is included immediately to the extent that the benefits are already vested, and otherwise is amortized on a straight-line basis over the average period until the benefits become vested.

The retirement benefit obligation recognized in the balance sheet represents the present value of the defined benefit obligation as adjusted for unrecognized actuarial gains and losses and unrecognized past service cost, and as reduced by the fair value of plan assets. Any asset resulting from this calculation is limited to the net total of unrecognized actuarial losses and past service cost, plus the present value of future available refunds and reductions in future contributions to the plan.

No other long-term or short-term benefits are granted to employees with the exception of warrants.

### **Share-based compensation**

The Group operates equity-settled, share-based compensation plans through which it grants share options (options giving the holder the right to subscribe to a specific number of shares in accordance with the share option plan, hereafter referred to as 'warrants') to employees and consultants and executive members of the board of directors. The fair value of the employee services received in exchange for the granting of the warrants is recognized as an expense over the vesting period with a corresponding increase in equity.

The total amount to be expensed over the vesting period is determined by reference to the fair value of the warrants granted, measured using the Black/Scholes model, taking into account the term and conditions upon which the warrants were granted excluding the impact of any non-market vesting conditions. At each balance sheet date, the entity revises its estimates of the number of warrants that are expected to become exercisable except where forfeiture is only due to shares not achieving the threshold for vesting. It recognizes the impact of the revision of original estimates, if any, in the income statement, and a corresponding adjustment to equity over the remaining vesting period. The proceeds received, net of any directly attributable transaction costs, are credited to share capital (nominal value) and share premium when the warrants are exercised.

The Group has opted to use the exemption to apply IFRS 2 Share-based Payment not apply to warrants granted after November 7, 2002, acquired before January 1, 2005.

## **(o) Financial instruments**

Financial assets and financial liabilities are included in the Group's balance sheet when the Group becomes a party to the contractual provisions of the instrument.

## 1. Non-derived financial instruments

### Trade receivables

When initially recognized, trade receivables are measured at fair value, and are subsequently measured at amortized cost using the effective interest rate method. Appropriate allowances for estimated irrecoverable amounts are included in the income statement when there is objective evidence that the asset is impaired. The allowance included is measured as the difference between the carrying amount of the asset and the present value of estimated future cash flows discounted at the effective interest rate computed at initial recognition.

### Investments

The investments are held as available for sale and annual closing date stated at market value. The fair value adjustment is included in other reserves until the investment is derecognized or has been impaired. The impairment is included in the income statement.

### Cash and cash equivalents

Cash and cash equivalents comprise cash on hand and demand deposits and other short-term, highly liquid investments (with less than six months to maturity) that are readily convertible into a known amount of cash and are subject to an insignificant risk of fluctuations in value.

### Financial liabilities and equity

Financial liabilities and equity instruments issued by the Group are classified according to the substance of the contractual arrangements entered into and the definitions of a financial liability and an equity instrument. An equity instrument is any contract that evidences a residual interest in the assets of the Group after deducting all its liabilities. The accounting policies adopted for specific financial liabilities and equity instruments are set out below.

### Trade payables

Trade payables are initially measured at fair value, and are subsequently measured at amortized cost, using the effective interest rate method.

### Equity instruments

Equity instruments issued by the Group are recorded at the proceeds received. Direct issue costs are processed as a deduction on equity.

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## **2. Derivative financial instruments**

The Group has a policy of not engaging in speculative transactions, nor does it issue or hold financial instruments for trading purposes.

Derivatives are initially recorded at cost and revalued at fair value on subsequent reporting dates.

### Impairment of financial assets

Financial assets are assessed for impairment on the balance sheet date. Financial assets are subject to impairment when it can be objectively established that the estimated future cash flows from the investments are affected by one or more events arising after the financial asset was initially recorded.

The carrying amount of the financial assets is directly reduced by the impairment loss, with the exception of trade receivables. For trade receivables, the carrying amount is reduced by means of a separate write-down account. If a trade receivable is considered uncollectable, it is written off in respect of this write-down account. Subsequent collection of amounts that had been previously written off are credited in respect of this write-down account. Modifications in the carrying amount of the write-down account are recognized in the income statement.

### **(p) Financial income and expenses**

Financial income includes interest income on invested funds. Interest income is recognized in the profit and loss account by using the effective interest method.

### **(q) Loss per share**

Basic net loss per share is computed based on the weighted average number of ordinary shares outstanding during the period.

Diluted net loss per share is computed based on the weighted average number of ordinary shares outstanding including the dilutive effect of warrants and options.

### **(r) Accounting for share-based payment transactions with parties other than employees**

For share-based payment transactions with parties other than employees, the Group measures the goods or services received, and the corresponding increase in equity, directly at the fair value of the goods or services received, unless that fair value cannot be estimated reliably. In the latter case, the goods or services received are measured at the fair value of the equity instruments granted using the Black/Scholes valuation model.

### **(s) Segment reporting**

A segment is a distinguishable component of the Group that is engaged either in providing specific products or services (business segment), or in providing products or services within a particular economic environment (geographical segment), which is subject to risks and rewards that are different from those of other segments.

## 6.2.4. Financial risk management

### (a) Capital management

The Group manages its capital with the aim of ensuring that the Group can continue to operate in continuity. At the same time, the Group wishes to ensure the return for its stakeholders via the results of its research activities, as well as perpetuating the increase in the value of the shares. This strategy has not changed compared to previous years.

The capital structure of the Group consists of financing debts (which the Group does not have at the moment), investments, cash and cash equivalents, as indicated in note 2.23 and note 2.24, and equity attributable to the equity holders of the Company, including capital, reserves and results carried over, as indicated in Notes 2.27 and 2.28 respectively.

The Group manages its capital structure and makes the necessary adjustments in the light of changes in economic circumstances, the risk characteristics of the underlying assets and the projected cash requirements of current research activities. When assessing the capital structure, the current cash position and projected cash burn are used as the key parameters. Cash burn is defined as the net result corrected for depreciation and amortization and less investments in fixed assets.

The Group wishes to maintain a capital structure that is sufficient to fund research activities during a period of at least twelve months. Currently, the cash inflows from possible cooperation or other cash generating activities are not taken into account here.

The Group is not subject to any externally imposed capital requirements.

### (b) Main accounting principles

Details of the main accounting principles and methods, including the inclusion criteria, the valuation basis and the basis on which income and costs are recognized, for each category of financial assets, liabilities and equity instruments, are explained under 2.3.

### (c) Categories of financial instruments

The only financial instruments the Company currently holds, are the so-called "loans and receivables" (including the cash and cash equivalents) and investments (refer to note 2.23 and note 2.24) amounting to 58.9 million EUR (2007: 48.4 million EUR). The investments are classified as "available for sale" as ThromboGenics has no intention of holding the investments until maturity.

### Objectives of financial risk management

The financial department of the parent company coordinates access to the national and international financial markets, and considers and manages the financial risks relating to the activities of the Group. However, these risks are confined to a minimal exchange rate risk. For the rest, there are no risks worth mentioning, such as liquidity risks or interest rate risks as the Group has virtually no debts and an ample cash position. The Group does not buy or trade in financial instruments for speculative purposes.

#### (d) Market risk

The Group's activities are such that the Group's income is exposed first and foremost to financial risks arising from exchange rate fluctuations. The Group aims to compensate the in and out flows in foreign currency. A substantial proportion of the research expenditure is invoiced in USD and GBP.

##### Analysis of sensitivity to exchange rates

The Group is mainly exposed to fluctuations in the pound sterling (GBP) and the US dollar (USD) against the Euro.

The table below shows sensitivity to a reduction of 10% in the Euro compared with the relevant foreign currencies. Management believes that 10% is a reasonable estimate of a possible fluctuation in foreign currencies.

The sensitivity analysis comprises the impact of a 10% decrease of the Euro against the foreign currency for, on the one hand the outstanding monetary items in foreign currencies at the end of the year, and on the other hand all transactions in foreign currencies (USD and GBP) over the entire year. A positive (negative) amount in the table below indicates that a decrease of 10% of the Euro against the relevant foreign currencies results in an increase (decrease) of the result of the year. An increase of 10% in the value of the Euro compared with the same currencies would have an equivalent but opposite impact on the results.

	USD impact			GBP impact		
	2008	2007		2008	2007	
Result outstanding items	+22	+79	(i)	429	47	(ii)
Result on all transactions over the year	-347	-284	(iii)	-210	-458	(iv)

i). The decrease of the positive effect is attributed to the decrease of the outstanding positions in USD compared to last year.

ii). The increase of the positive effect is explained by an increase of the outstanding position in GBP compared to last year.

iii). The negative effect is reinforced by the larger number positions in USD through the year in comparison with last year.

iv). The decrease in the positions in GBP through the year reduces the negative effect compared to last year.

The management believes that the above sensitivity analysis provides a faithful picture of the risk that the Group incurs during the year in respect of exchange rate fluctuations.

#### (e) Interest risk management

The Group does not have any external debt financing at the moment. Furthermore, the Group does not have any contracts with a variable interest rate. Consequently, there is currently no need for a specific interest risk management policy in the Group.

**(f) Credit risk management**

Credit risk relates to the risk that a counter party will fail to fulfil their contractual obligations with the result that Group would suffer a loss. The Group's policy focuses on only working with creditworthy counterparties and, where necessary, requiring adequate securities. Information about the creditworthiness of counterparties is provided by independent ratings agencies and, if this is not available, the Group uses information that is publicly available as well as its own internal records. Credit risk is managed by the financial department of the parent company by means of individual follow-up of credit per counterparty.

Given the Group's limited number of clients, the Group is not subject to significant concentrations of credit risk. We refer to the table in Note 2.22.

The credit risk on cash investments is limited given that the counterparties are banks with high credit scores attributed by international rating agencies.

**(g) Liquidity risk management**

The Group manages its liquidity risk by ensuring adequate reserves and by constantly checking the projected and actual cash flows. At the moment the Group is not subject to any substantial liquidity risk.

**6.2.5. Main accounting estimates and assessments**

Drawing up the financial statements in accordance with IFRS obliges the management to use estimates and assumptions that impact on the amounts reported under assets and liabilities, the notes on the latent assets and liabilities on the date of the financial statements, and the reported amounts of income and expenditure in the course of the reporting period. The actual results may differ from these estimates.

The main assumptions relating to future developments and the main sources of uncertainty as regards estimates on the balance sheet dates are set out below.

**Share-based payment schemes**

The Group defines the cost of share-based payment schemes on the basis of the fair value of the equity instrument on the date of issue. Estimating the fair value involves choosing the most suitable valuation model for these equity instruments, and the characteristics of the issue have a decisive impact. It also assumes the input in the valuation model of a number of relevant assessments, such as the estimated useful life of the option, volatility, etc. The assessments and the model are specified in more detail in Note 2.29.

**Pension obligations**

The cost of a defined benefit plan is determined on the basis of actuarial valuations. An actuarial valuation involves estimating discount rates, expected returns on assets, future salary increases, mortality figures, and future pension increases. Due to the long-term nature of these pension plans, valuation is subject to considerable uncertainty. We refer to Note 2.30 for additional details.

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## Intangible assets

The Group enables development as intangible assets if the conditions for the recognition of developed intangible assets are met, otherwise such costs are included in the income statement when they arise. The costs are capitalized only if the product is in phase III and the chances of future success are highly estimated.

### 6.2.6. Segment information

The Group believes that the current R&D programmes and the geographic areas involve similar risks, and that consequently there is only one business and geographical segment.

### 6.2.7. Revenue

#### License income

In June 2008, ThromboGenics and its partner BioInvent granted a worldwide exclusive license to F. Hoffmann La Roche AG for the development and commercialisation of their jointly developed antibody TB-403. In 2008, Roche paid to ThromboGenics and BioInvent a non-refundable upfront payment of 50 million Euro, of which ThromboGenics received 30 million Euro as its share.

The remaining revenue is primarily related to other agreements with pharmaceutical companies on the P1GF product.

#### Other income

Other income consists mainly of the sale of various reagents including media and cell lines.

### 6.2.8. Cost of sales

In thousands of Euro (years ended 31 December)

	2008	2007
Cost of the sale of reagents	(47)	(168)
Manufacturing rights F-Hoffmann La Roche AG	(2,700)	
<b>Total cost of sales</b>	<b>(2,747)</b>	<b>(168)</b>

ThromboGenics NV made a payment of 2.7 million Euro to the VIB. We refer to note 2.32 for further information about this transaction.



### 6.2.9. Research and development expenses

In thousands of Euro (years ended 31 December)

	2008	2007
Employee benefits	(3,361)	(3,013)
Subcontracted R&D activities	(9,691)	(11,478)
Reagents and materials	(510)	(417)
Patent expenses	(262)	(331)
Consultancy and other	(1,483)	(1,661)
Subtotal	(15,307)	(16,900)
Depreciation and amortization	(405)	(332)
<b>Total research and development expenses</b>	<b>(15,712)</b>	<b>(17,232)</b>

The research and development expenses mainly relate to expenses of the pre-clinical research and phase I and II clinical studies.

### 6.2.10. General and administrative expenses

In thousands of Euro (years ended 31 December)

	2008	2007
Employee benefits	(675)	(544)
Depreciation and amortization	(24)	(4)
Other	(2,332)	(1,767)
<b>Total general and administrative costs</b>	<b>(3,031)</b>	<b>(2,315)</b>

The other administration expenses mainly include consultancy and professional fees, general expenses and computer and equipment expenses.

### 6.2.11. Selling expenses

In thousands of Euro (years ended 31 December)

	2008	2007
Employee benefits	(460)	(374)
Other	(33)	(39)
<b>Total selling expenses</b>	<b>(493)</b>	<b>(413)</b>

## 6.2.12. Other operating income

In thousands of Euro (years ended 31 December)	2008	2007
Government grants	524	735
Income from recharge of costs	1,625	473
<b>Total other operating income</b>	<b>2,149</b>	<b>1,208</b>

The income from recharge of costs relates to research and development expenses recharged to BioInvent.

## 6.2.13. Financial Income

In thousands of Euro (years ended 31 December)	2008	2007
Income from short-term investments	27	31
Other interest and similar benefits	2,113	1,604
Exchange rate gain on USD and GBP bank accounts	1,173	145
Other	35	
<b>Total financial income</b>	<b>3,348</b>	<b>1,780</b>

The other interests are related to received and accrued interest on investments.

## 6.2.14. Financial expenses

In thousands of Euro (years ended 31 December)	2008	2007
Bank costs	(20)	(17)
Impairment on short-term financial investments	(82)	(33)
Other	(3)	-
Exchange rate loss on USD and GBP bank accounts	(1,645)	(271)
<b>Total financial expenses</b>	<b>(1,750)</b>	<b>(321)</b>

## 6.2.15. Employee benefits

In thousands of Euro (years ended 31 December)	2008	2007
Wages, salaries and bonuses	(3,740)	(3,062)
Share-based compensation expenses (Note 2.28)	(702)	(862)
Pension costs – defined benefit plan (Note 2.29)	(54)	(7)
<b>Total</b>	<b>(4,496)</b>	<b>(3,931)</b>

The average number of full-time equivalents (including executive directors) was as follows:

In numbers	2008	2007
Selling	2	2
Research and development	34	21
Administration	6	9
<b>Total</b>	<b>42</b>	<b>32</b>

The share-based compensation expense included in the income statement as such is given below:

In thousands of Euro (years ended 31 December)	2008	2007
Research and development expenses	280	569
General and administrative expenses	306	179
Selling expenses	116	114
<b>Total</b>	<b>702</b>	<b>862</b>

The fair value of each warrant is assessed on the basis of the Black & Scholes model on the date it is granted, taking into account the following assumptions:

	Warrants granted				
	2008	2007			
	July 2008	November 2007	July 2007	May 2007	February 2007
Number of warrants granted	340,667	8,000	8,000	16,000	42,000
Current share price on date of acceptance (in Euros)	8.65	9.30	10.57	11.10	11
Exercise price	8.65	9.05	11.12	10.82	11.05
Expected dividend yield	-	-	-	-	-
Expected stock price volatility	50%	70%	70%	70%	70%
Risk-free interest rate	4.17%	3.99%	4.46%	4.23%	3.88%
Expected duration	2.5	2.5	2.5	2.5	2.5
Fair value	2.92	3.77	4.06	4.51	4.91

Since July 2006 the closing price on the stock market of Euronext Brussels is used **as a reference** for the current share price on date of acceptance.

The **estimated volatility** is based on the historical volatility of similar biotech companies that operate in the same disease areas as the Group, or that are similar in size or activity. In 2008 the volatility was adjusted based upon the average of all Belgian Biotech companies.

The **expected duration** is calculated as the estimated duration until exercise, taking into account the specific features of the plans.

The weighted average **risk-free interest rates** used are based on the Belgium government bond rates at the date of granting with a term equal to the expected life of the warrants.

The Group has also granted warrants to parties that are not employees of the Group. As the services rendered are of such a specific nature that the fair value cannot be determined reliably, ThromboGenics NV has determined the fair value of the services received from these parties by reference to the warrants granted.

## 6.2.16. Operational leases

In thousands of Euro (years ended 31 December)	2008	2007
Leasing payments included as an expense (lessee)	202	168

## 6.2.17. Taxes

Taxes in the profit and loss account.

In thousands of Euro (years ended 31 December)	2008	2007
Foreign tax	(90)	(9)
<b>Total</b>	<b>(90)</b>	<b>(9)</b>

Belgian income tax is calculated at 33.99 per cent of the results of the year. The taxes for other jurisdictions are calculated at applicable tax rates in the relevant jurisdiction.

A reconciliation explaining the difference between the expected income tax of the Group and the actual income tax is as follows:

In thousands of Euro (years ended 31 December)	2008	2007
Expected tax credit (cost), calculated by applying the Belgian statutory tax rates to the accounting profit/loss	(4,142)	5,427
Effect of differing tax rates of subsidiaries operating in different jurisdictions	(307)	(238)
Use of notional interest for the year 2008 of ThromboGenics NV	866	-
Use of notional interest and cumulative losses of ThromboGenics NV for which no deferred tax asset was recorded in the past	3,961	
Non-included deferred tax receivables	(188)	(5,594)
Other	(280)	396
<b>Actual Taxes</b>	<b>(90)</b>	<b>(9)</b>

The main difference between the theoretical income tax and the actual income tax is explained by deferred tax receivables on tax transferable losses, for which management believes that they will not be recorded in the near future and which are therefore not included.

## 6.2.18. Result per share

### Basic earnings per share

Weighted average number of ordinary shares in the calculation of basic earnings per share by December 31, 2008 is based on the holders of ordinary shares attributable profit / (loss) from 12,095 K Euro (2007: (15,967) K Euro) and a weighted average number of ordinary shares outstanding during 2008 of 25,641,020 (2007: 23,935,960), calculated as follows:

	2008	2007
Issued ordinary shares per 1 January	25,502,160	22,140,305
Effect of capital increase through issue of shares	-	1,449,735
Effect of exercised share options	138,860	345,920
Average number of ordinary shares per 31 December	25,641,020	23,935,960
In thousands of Euro, except for result per share		
Net result	12,095	(15,967)
Basic result per share	0.47	(0.67)

### Diluted earnings per share

The calculation of diluted earnings per share by December 31, 2008 is based on the holders of ordinary shares attributable profit / (loss) from 12,095 K Euro (2007: (15,967) K Euro) and a weighted average number of ordinary shares adjusted for all potential dilutive effects on the ordinary shares outstanding during 2008 of 26,847,249 (2007: 25,905,104), calculated as follows:

	2008	2007
Issued ordinary shares (diluted) per 1 January	26,667,531	24,403,501
Effect of capital increase through issue of shares		1,449,735
Effect of share options on issue	179,718	51,868
Average number of ordinary shares (diluted) per 31 December	26,847,249	25,905,104
In thousands of Euro, except for result per share		
Net result	12,095	(15,967)
Diluted result per share	0.45	(0.62)

The Group has granted warrants to employees, consultants and directors to buy ordinary shares.

See Note 2.28 for an overview of the number of outstanding warrants at each year end.

## 6.2.19. Property, plant and equipment

	Machines, plant and equipment	Furniture and fittings	Total
<b>As at 1 January 2007</b>			
Cost	1,484	645	2,129
Accumulated depreciation	(1,001)	(598)	(1,599)
Net carrying amount	483	47	530
<b>Year ended 31 December 2007</b>			
Additions	618	248	866
Disposals		(3)	(3)
Depreciation expenses	(269)	(68)	(337)
Retirements		1	1
Net carrying amount	832	225	1,057
<b>As at 31 December 2007</b>			
Cost	2,102	893	2,995
Accumulated depreciation	(1,270)	(668)	(1,938)
Net carrying amount	832	225	1,057
<b>Year ended on 31 December 2008</b>			
Additions	310	116	426
Disposals	(86)	(16)	(102)
Depreciation expenses	(311)	(118)	(429)
Retirements	37	15	52
Net carrying amount	782	222	1,004
<b>As at 31 December 2008</b>			
Cost	2,326	993	3,319
Accumulated depreciation	(1,544)	(771)	(2,315)
Net carrying amount	782	222	1,004

There are still property, plant and equipment worth 1,3 million Euro in use that have already been written off in full. No property, plant and equipment is pledged or in limited use.

In 2008, a number of not fully written off fixed assets have been sold. The added value on these sales is recorded as other income.

## 6.2.20. Intangible assets

<b>As at 1 January 2008</b>	
Cost	-
Accumulated depreciation	-
Net carrying amount	-
<b>Year ended 31 December 2008</b>	
Additions	2,092
Disposals	-
Depreciation expenses	-
Net carrying amount	2,092
<b>As at 31 December 2008</b>	
Cost	2,092
Accumulated depreciation	-
Net carrying amount	2,092

For the first time during the current financial year 2008, the company has incurred costs which relate to development in the context of Phase III of clinical trials with microplasmin. For the implementation of these studies, which will take place in the United States, Europe and North America, the company contracted with Chiltern Ltd and Chiltern Inc. The production agreement for microplasmin has been outsourced to Avecia Ltd. These costs will be capitalized as intangible assets, given the high probability of commercialization (analysts estimate the probability of success between 65% and 75%) and the fact that the product is already in Phase III.



## 6.2.21. Goodwill

In thousands of Euro

<b>As at 1 January 2007</b>	
Cost	2,586
Accumulated impairment losses	-
Net carrying amount	2,586
<b>Year ended 31 December 2007</b>	
2,586	
Additions	-
Disposals	-
Impairment losses	-
Net carrying amount	2,586
<b>As at 31 December 2007</b>	
Cost	2,586
Accumulated impairment losses	-
Net carrying amount	2,586
<b>Year ended 31 December 2008</b>	
2,586	
Additions	-
Disposals	-
Impairment losses	-
Net carrying amount	2,586
<b>As at 31 December 2008</b>	
Cost	2,586
Accumulated impairment losses	-
Net carrying amount	2,586

This goodwill relates to the historic acquisition of an ownership interest in Thromb-X NV.

As the Group only operates in one business segment, the management has decided for management purposes to follow goodwill at Group level.

Management estimates that the average closing price of the Euronext over the year 2008 (EUR 8.22), multiplied by the number of ordinary shares (25,730,789, see Note 2.27) is a reasonable indicator of the fair value of the Group. Consequently, the management has no indication of a possible impairment loss on the above goodwill.

## 6.2.22. Trade and other receivables

In thousands of Euro (years ended 31 December)	2008	2007
Trade receivables	712	397
Other receivables	78	211
Prepaid expenses and other current assets	813	438
Tax receivables	823	487
Tax credit	101	
<b>Total</b>	<b>2,527</b>	<b>1,533</b>

The average number of days client credit is 30 days. Trade receivables are booked on the basis of an estimate of non-collectable amounts, taking into account the payment history of the other party.

The table below shows the balance sheet of the key counterparties on the balance sheet date:

In thousands of Euro (years ended 31 December)	2008	2007
BioInvent	439	235
F. Hoffmann La Roche AG	116	
LSRP	61	
Biosite	32	
Millipore	29	22
American Diagnostica	20	
Other trade receivables	15	4
Rhein Minapharm		136
<b>Total</b>	<b>712</b>	<b>397</b>

A total of 96% (2007: 99.5%) of these trade receivables relate to non-due trade receivables. Management has sufficient confidence in the creditworthiness of the counterparty, and the amounts are considered collectable in full. The Group has no securities linked to these receivables.

When determining the collectability of a trade receivable, the Group takes into account any change in the quality of the receivable between the date on which the credit was granted and the reporting date. The directors believe that there is no need to write off any trade receivables.

The prepaid expenses and other current assets consist primarily of the following elements: interest receivable (322,875 Euro), grants income receivable (106,955 Euro) and other prepaid expenses in relation to maintenance, insurance and conferences (383,409 Euro).

The outstanding tax claims relate to recoverable VAT and withholding tax on interest.

The tax credit applies to the acquired intangible assets.

## 6.2.23. Investments

In thousands of Euro (years ended 31 December)

	2008	2007
Government bonds	82	84
Other investments	28,483	6,626
<b>Total investments</b>	<b>28,565</b>	<b>6,710</b>

### Financial Assets according to categories as defined in IAS 39

	Available for sales
<b>Balance Sheet as at 1 January 2008</b>	<b>6,710</b>
Exchange rate differences	-
Additions	22,044
Retirements	-
Impairments	(82)
Appreciation at market value	(107)
<b>Balance Sheet as at 31 December 2008</b>	<b>28,565</b>
-/- of which taken in fixed assets	-
Taken in current assets	28,565
<b>Composition</b>	
- EUR Defensive Strategy CPPI	2,000
- 1Y EUR Accrual note	2,000
- KBC Ifima – 18 month public FRN issue	3,000
- KBC D-Star Corporate note1	11,000
- KBC Arcade Corporate note 1	10,000
- Other bonds	754
-/- Impairments	(82)
-/- Appreciation at market value	(107)
<b>Total</b>	<b>28,565</b>
<b>Breakdown per currency</b>	
- in Eur	28,301
- in other currency	264
<b>Total</b>	<b>28,565</b>

All investments have a 100% capital guarantee with the exception of the EUR Defensive Strategy CPI with 95% capital guarantee. As ThromboGenics NV does not have the intention to keep investments until maturity, the investments are being classified as “available for sale.” The investments at year-end are valued at fair market value and the resulting difference is recognized in equity.

The EUR Defensive Strategy CPPI and the 1Y EUR Accrual note have been issued by ING. All KBC related products have been issued by KBC Asset Management. The remaining bonds are held by Coutts Bank and distributed in 17 bonds of private and public institutions. In 2007 there was 6,710 K EUR recognized as "held to maturity". The transfer to "Available for sales" had only a small impact.

### 6.2.24. Cash and cash equivalents

In thousands of Euro (years ended 31 December)	2008	2007
Cash	30,356	40,111
Total cash and cash equivalents	30,356	40,111

### 6.2.25. Other short-term liabilities

In thousands of Euro (years ended 31 December)	2008	2007
Employee benefits	314	241
Accruals regarding grants	89	275
Accruals	542	
Total other short-term liabilities	945	516

The other current liabilities have a significant increase over last year. The increase relates to a single agreement for the sale of the ES Cell Data Bank for an amount of 450,000 Euro. This amount was not recognized in sales in December 31, 2008 because not all criteria relating to revenue recognition were met on December 31, 2008.

### 6.2.26. Deferred taxes

The following temporary differences which might give rise to deferred taxes relate to:

In thousands of Euro (years ended 31 December)	2008	2007
Net tax loss carry forward	36,916	49,713
Pension accrual	(12)	(13)
Notional interest deduction		1,855
Total deductible temporary differences	36,904	51,555
Non included deferred tax receivables	11,071	11,259

The tax loss carry forward can be offset by future gains recorded by the Group for an indefinite period. Given the uncertainty about whether the Group is in a position to record tax gains in the near future, the Group has not included a deferred tax receivable.

## 6.2.27. Share capital

As at 31 December 2008 ThromboGenics NV had 25,730,789 ordinary bearer shares without indication of nominal value. All the shares are fully paid up and all have the same rights.

The General Meeting of 7 June 2006 granted the Board of Directors the authority, in the context of the authorized capital, and for a maximum period of five years, to increase the capital of the company on one or more occasions by a maximum of 99,643,314.50 Euro. This authority granted to the Board of Directors applies to capital increases by contributions in cash or in kind, by conversion of reserves, with or without the issue of new shares. Within the limits of the authorized capital, the Board of Directors can also issue convertible bonds or warrants.

The modification of the number of shares in the course of each of the two years ended on 31 December 2008 was as follows:

Number of shares	
31 December 2006	22,140,305
Capital increase by contribution in cash – issue of new ThromboGenics NV shares	2,214,030
Capital increase by contribution in kind – issue of new ThromboGenics NV shares	1,127,825
Capital increase – exercising warrants	20,000
31 December 2007	25,502,160
Capital increase by contribution in kind – issue of new ThromboGenics NV shares	172,629
Capital increase – exercising warrants	56,000
31 December 2008	25,730,789

The following significant transactions relating to shares in the Group and its capital in the two years ended on 31 December 2007 and 31 December 2008:

- On 7 May 2007, a capital increase took place in the context of the authorized capital by a contribution in cash and with the issue of 2,214,030 new ThromboGenics NV shares.
- On 13 September 2007, a capital increase took place in the context of the authorized capital by means of a contribution in kind of 1,127,825 ThromboGenics Ltd shares and with the issue of 1,127,825 new ThromboGenics NV shares. The ThromboGenics Ltd shares brought in were created as a consequence of the conversion of warrants at ThromboGenics Ltd. We refer to the table below for more information.
- On 13 September 2007, a capital increase took place in the context of the authorized capital by the conversion of 20,000 warrants. We refer to the table below for more information.
- On 8 April 2008 a capital increase took place in the context of the authorized capital by means of a contribution in kind of 172,629 ThromboGenics Ltd shares and with the issue of 172,629 new ThromboGenics NV shares. The ThromboGenics Ltd shares brought in were created as a consequence of the conversion of warrants at ThromboGenics Ltd. We refer to the table below for more information.
- On 10 October 2008, a capital increase took place in the context of the authorized capital by the conversion of 56,000 warrants. We refer to the table below for more information.

The share capital and the 'issue premium' account evolved as a result of the transactions listed above as follows:

In thousands of Euro	Capital	Issue premium
<b>31 December 2006</b>	<b>95,974</b>	<b>0</b>
Capital increase by contribution in cash issue of ThromboGenics NV shares	9,965	13,947
Costs of capital increase	(772)	
Capital increase by contribution in kind – issue of ThromboGenics NV shares	5,075	1,692
Capital increase – exercising warrants	90	8
Costs exercising warrants	(23)	
<b>31 December 2007</b>	<b>110,309</b>	<b>15,647</b>
Capital increase by contribution in kind – issue of ThromboGenics NV shares	777	86
Capital increase – exercising warrants	252	104
<b>31 December 2008</b>	<b>111,338</b>	<b>15,837</b>

The difference between the share capital, as indicated above, and the 'capital' account on the balance sheet consists of the costs relating to the various capital transactions (for a total of 4.464 K Euro), which in accordance with IAS 1 '*Presentation of the Financial Statements*' is deducted from the income from these capital transactions.

## 2.28. Other reserves

In thousands of Euro

<b>31 December 2006</b>	<b>(20,607)</b>
Conversion of warrants by ThromboGenics Ltd	5,036
Contribution in kind ThromboGenics Ltd shares	(6,767)
Share-based payment	862
<b>31 December 2007</b>	<b>(21,476)</b>
Conversion of warrants by ThromboGenics Ltd	893
Contribution in kind ThromboGenics Ltd shares	(863)
Share-based payment	702
Fair value adjustment	(107)
<b>31 December 2008</b>	<b>(20,851)</b>

On 13 September 2007 ThromboGenics Ltd exercised 1,127,825 options. The resultant shares were exchanged on the basis of one ThromboGenics Ltd share for one ThromboGenics NV share. By exercising these options the capital of ThromboGenics Ltd was increased by 5,035,789 Euro. The contribution of 1,127,825 shares in ThromboGenics NV was effected at 6,766,950 Euro.

On 8 April 2008 ThromboGenics Ltd exercised 172,629 options. The resultant shares were exchanged on the basis of one ThromboGenics Ltd share for one ThromboGenics NV share. By exercising these options the capital of ThromboGenics Ltd was increased by EUR 893,277. The contribution of 172,629 shares in ThromboGenics NV was effected at EUR 863,145.

The fair value adjustment for financial assets available for sales, an amount of 107 K Euro, includes the cumulative net change in fair value of available-for-sale financial assets until the assets are derecognized or have been impaired.

## Share-based payment schemes

The Group has created various groups of warrants that can be granted to employees, directors, consultants and research institutions. Until the creation and subsequent public listing of ThromboGenics NV, warrant plans were created in respect of ThromboGenics Ltd. Since then, the public listing warrant plans have been created in respect of ThromboGenics NV.

The warrants issued in the context of ThromboGenics Ltd warrant plans can still be exercised and converted into ThromboGenics Ltd shares. However, the terms and conditions of these warrant plans were altered by the flotation of the Group on the stock market: the ThromboGenics Ltd shares created are immediately entered into the capital of ThromboGenics NV in exchange for shares in the latter (capital increase by contribution in kind).

On 19 December 2007, the general meeting of option holders of ThromboGenics Ltd decided to modify the terms and conditions of the exercising existing warrants under Irish warrant plans described below. Only two exercise windows now apply for these warrants: March 2008 and March 2009. All warrants that are not exercised on this date will automatically be declared null and void.

Synoptic overview of all outstanding warrants granted between 1999 and 31 December 2008

Creation date of scheme	Total number created	Date granted	Total number granted	Exercise price (in Euros)	Beneficiary
Unapproved scheme 2003	See description below	2000- 2005	1,786,745	Between 1.27 – 6.35	Employees, key consultants and directors of the Group.
Approved scheme 2003	See description below	2003- 2004	55,546	Between 1.27 – 6.35	Employees, key consultants and directors of the Group
Warrants scheme Belgium 2006	500,000	2006-2007	444,000	between 4.91 en 11.12	Employees, key consultants and directors of the Group
Warrants scheme Belgium 2008	450,000	2008	340,667	8.65	Employees, key consultants and directors of the Group

## ThromboGenics Limited Unapproved Employees Share Option Scheme

ThromboGenics Ltd adopted the ThromboGenics Limited Unapproved Employee Share Option Scheme (the "Unapproved Scheme") as of 30 November 2002. Under the Unapproved Scheme, ThromboGenics Ltd, through the Remuneration Committee, may grant warrants to eligible employees (i.e. every employee or director of ThromboGenics Ltd or any of its subsidiaries or any other person selected by the Remuneration Committee). Since the launch of the public company ThromboGenics NV, no warrants have been granted under this plan.

Warrants may be granted to eligible employees through this Scheme between 30 November 2002 and its tenth anniversary. The number of warrants to be granted under the Unapproved Scheme is limited to the extent that a warrant may not be granted if the result of granting the warrant would be that the number of ordinary shares in the company placed under warrant under the Unapproved Scheme or any other discretionary share option scheme established by ThromboGenics Ltd would exceed 20 per cent of the issued share capital of ThromboGenics Ltd.



The exercise price of the warrants granted is not less than the market value of the underlying share, or, if higher, the nominal value of the underlying share. A warrant under the Unapproved Scheme may not be exercised earlier than the last of the first anniversary of the date of grant, or any relevant date specified in the granting conditions as expressed in the warrant certificate. Thereafter the warrant shall become exercisable in respect of a further one third on each of the anniversaries of such date. In any case, a warrant may not be exercised more than ten years after the date of granting, and any warrant not exercised by that time shall lapse immediately. The vesting conditions are conditional on the beneficiary remaining in the entity's employment for a specified period of time defined by the Remuneration Committee on a case by case basis.

### **ThromboGenics Limited Revenue Approved Employee Share Option Scheme**

ThromboGenics Ltd adopted the ThromboGenics Limited Revenue Approved Employee Share Option Scheme (the "Approved Scheme") as of 30 November 2002. Under the Approved Scheme, ThromboGenics Ltd, through the Remuneration Committee, may grant warrants to eligible employees (i.e. every person who on the date of granting and the date of exercise is a full time director – other than a non-executive director – or an employee of ThromboGenics Ltd or any of its subsidiaries who is liable for tax in respect of such office or employment under Schedule E of the TCA Taxes Consolidation Act ("TCA") of 1997 in Ireland).

Warrants may be granted to eligible employees through this Scheme between 30 November 2002 and its tenth anniversary. The number of warrants to be granted under the Approved Scheme are limited to the extent that a warrant may not be granted if the result of granting the warrant would be that the number of ordinary shares in the company placed under warrant under the Approved Scheme or any other discretionary share option scheme established by ThromboGenics Ltd would exceed 20 per cent of the issued share capital of ThromboGenics Ltd. In addition, under the Approved Scheme the number of warrants granted must correspond to the stipulations of paragraph 8 of Schedule 12C of the TCA 1997. This paragraph basically stipulates that in order for the scheme to have the benefit of favourable tax treatment, the scheme must be eligible for all Irish tax resident employees and the offer of warrants is made on similar terms to all Irish tax resident employees. Since the launch of the public company ThromboGenics NV, no warrants have been granted under this plan.

The exercise price under the Approved Scheme shall be not less than the market value of the underlying share, or, if higher, the nominal value of the underlying share. A warrant under the Approved Scheme may not be exercised earlier than the last of the first anniversary of the date of grant, or any relevant date specified in the granting conditions as expressed in the warrant certificate. In addition, a warrant shall only become exercisable in respect of one third at these dates. Thereafter the warrant shall become exercisable in respect of a further one third on each of the anniversaries of such date. In any case, a warrant may not be exercised more than ten years after the date of grant and any warrant not exercised by that time shall lapse immediately. The vesting conditions are conditional on the beneficiary remaining in the entity's employment for a specified period of time defined by the Remuneration Committee on a case by case basis.

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### **Belgium 2006 warrant plan**

On 7 June 2006, the General Meeting of ThromboGenics NV decided to issue the Belgium 2006 warrant plan. Under this warrant plan a maximum of 500,000 warrants can be issued and granted to employees, directors and consultants of the Group. Each warrant entitles the holder to subscribe to one ThromboGenics NV share.

Warrants are granted under this plan by the Board of Directors or the remuneration committee, except for directors. Authority for this lies with the General Meeting. Warrants are offered free of charge or in return for payment. The exercise price is equal to the lower of (i) the average of the closing prices of the share on the stock market during the 30 days prior to the offering of a warrant or (ii) the closing price on the last stock market day prior to the offer. Warrants granted under this plan are valid for five years. The conditions under which a warrant holder is entitled to exercise a warrant are established by the remuneration committee. The right to exercise may depend on the achieving certain results, or remaining in the employment of the Group, or any other condition.

### **Belgium 2008 warrant plan**

On 6 May 2008, the General Meeting of ThromboGenics NV decided to issue the Belgium 2008 warrant plan. Under this warrant plan a maximum of 450,000 warrants can be issued and granted to employees, directors and consultants of the Group. Each warrant entitles the holder to subscribe to one ThromboGenics NV share.

Warrants are granted under this plan by the Board of Directors or the remuneration committee, except for directors. Authority for this lies with the General Meeting. Warrants are offered free of charge or in return for payment. The exercise price is equal to the lower of (i) the average of the closing prices of the share on the stock market during the 30 days prior to the offering of a warrant or (ii) the closing price on the last stock market day prior to the offer. Warrants granted under this plan are valid for five years. The conditions under which a warrant holder is entitled to exercise a warrant are established by the remuneration committee. The right to exercise may depend on the achieving certain results, or remaining in the employment of the Group, or any other condition.

### **Other warrants**

On 1 August 2003, ThromboGenics Ltd entered into a consultancy agreement with a US consultant. Under the terms of this agreement, the consultant was granted 20,000 warrants at an exercise price of USD 3.82. 10,000 warrants vested on the first anniversary of the agreement and 10,000 on the second anniversary. In addition, a further 10,000 warrants were granted to the consultant on the condition that he assists the company in completing a deal with a minimum upfront cash component of USD 10 million. As no such deal has been concluded yet, these warrants have not been granted.

In addition, on 31 March 2004, the Company entered into a license and collaboration agreement with a third party. As part of the compensation due by the Company under this agreement, the Company will grant a total of 10,000 warrants to the founders of the contracting party on the condition that a commercial pharmaceutical deal in the microplasmin/vitreoretinal application with a minimum cash component of 10 million USD is signed. As no such deal has been concluded yet, these warrants have not been granted. The Company has not issued any other warrants with conditional grant dates.

Activity under the different share option plans for the two years ended 31 December was as follows:

	Total	Belgian Plan	Unapproved scheme	Approved scheme	Other warrants granted in 1999 en 2006
Outstanding as at 31 Dec 2006	2,263,196	370,000	1,200,745	42,451	650,000
Granted	74,000	74,000	-	-	-
Forfeited	(24,000)	(24,000)	-	-	-
Exercised	(1,147,825)	(20,000)	(468,096)	(9,729)	(650,000)
Outstanding as at 31 Dec 2007	1,165,371	400,000	732,649	32,722	-
Granted	340,667	340,667	-	-	-
Forfeited	(33,742)	-	(33,742)	-	-
Exercised	(228,629)	(56,000)	(151,201)	(21,428)	-
Outstanding as at 31 Dec 2008	1,243,667	684,667	547,706	11,294	-

Movements in the number of warrants outstanding and their related weighted average exercise prices are as follows:

	2008		2007	
	Average exercise price in EUR	Warrants	Average exercise price in EUR	Warrants
As at 1 Jan.	5.65	1,165,371	4.89	2,263,196
Granted	8.65	340,667	10.79	74,000
Forfeited	6.35	(33,742)	6.20	(24,000)
Exercised	5.47	(228,629)	4.47	(1,147,825)
As at 31 Dec.	6.48	1,243,667	5.65	1,165,371

Outstanding vested warrants (in thousands) as at 31 December 2008 have the following earliest exercise date, maturities and exercise prices:

Earliest exercise date	Expiry date	Exercise price	2008 (thousands)
2009	2009	€6.35	321
2009	2009	€3.13	95
2009	2009	\$3.82	143
2009	2011	€4.91	114
2009	2011	€6.20	148
2009	2011	€7.2	8
2009	2012	€11.05	42
2009	2012	€10.82	8
2009	2012	€11.12	8
2009	2012	€9.05	8
Total weighted average		5.62	895

## 6.2.29. Pension obligations

ThromboGenics offers its employees retirement benefits that are funded through a group insurance plan managed by an insurance fund. The insurance group plan is based on a “defined benefit” system. In a defined benefit pension plan, an employer commits to paying its employee a specific benefit for life beginning at his or her retirement. The amount of the benefit is known in advance, and is usually based on factors such as age, earnings, and years of service. Defined benefit plans do not have contribution limits, but they do have a limit on the maximum annual retirement benefit.

### Defined benefit scheme

The main assumptions used for the actuarial valuations were as follows:

	2008	2007
Discount rate	5.6%	5.3%
Expected return on plan assets	4%	4%
Expected rate of salary increases	5%	2.5%

The expected wage rate is adjusted to current inflation and the change in remuneration policy.

The calculation of the defined benefit scheme takes into account the MR / FR mortality tables and the risk of retirement. The medical cost trend rate and the pension increase rates were estimated at 0%.

The amount included in the balance sheet relating to the Group’s defined benefit plan is as follows:

In thousands of Euro	2008	2007
Cash value of the defined pension obligations	(357)	(165)
Fair value of the plan assets	208	111
<b>Net current value</b>	<b>(149)</b>	<b>(54)</b>
Non-included actuarial losses	222	93
<b>Net (liability) or receivable included in the balance sheet</b>	<b>73</b>	<b>39</b>

Amounts included in the income statement relating to the Group’s defined benefit plan are as follows:

In thousands of Euro	2008	2007
Current pension costs for the year	(43)	(34)
Interest costs	(8)	(13)
Expected return on plan assets	6	9
Actuarial losses included in the year	(9)	(7)
Past service costs		
Curtailments	0	38
<b>Total in costs for employees’ compensation</b>	<b>(54)</b>	<b>(7)</b>

Modifications in cash value of defined benefit obligations not covered by capital are as follows:

In thousands of Euro	2008	2007
Opening defined benefit obligation as at 1 January	(165)	(305)
Pension costs for the year	(43)	(34)
Employees' contribution	(23)	(22)
Interest costs	(8)	(13)
Actuarial losses	(124)	(17)
Curtailments or settlements	0	226
<b>Closing defined benefit obligation</b>	<b>(357)</b>	<b>(165)</b>

In 2008, we have a loss of Euro 123,648 to the promised pension obligations that can be explained as follows:

A loss of 79,185 Euro which is due to the change in the assumptions:

- Change in discount rate: 5.6% instead of 5.3%
- Change in inflation: 2.5% instead of 2%
- Change in salary increase: 5% instead of 2.5%

A loss of 44,464 Euro as a result of experience:

- Real salary increases different from the assumptions
- New connections

Changes in the fair value of plan assets are as follows:

In thousands of Euro	2008	2007
Opening value of plan assets	111	179
Expected return	6	9
Actuarial profits (losses)	(13)	(46)
Employer's contributions	88	75
Employees' contributions	23	22
Curtailments and settlements	0	(128)
Compensation paid	(6)	
<b>Closing fair value of plan assets</b>	<b>208</b>	<b>111</b>
<b>Actual return on plan assets</b>	<b>(7)</b>	<b>(37)</b>

The main categories of the plan assets as at 31 December are as follows:

In thousands of Euro	2008	2007
Insurance contracts	208	111
Fair value of the plan assets	208	111

The plan assets do not include any of our own financial instruments or any property owned by us.

Movements in the net liability included in the balance sheet are as follows:

In thousands of Euro	2008	2007
Opening net liability	39	(29)
Net expenses included in the income statement	(54)	(7)
Employer's contributions	88	75
Closing net (liability) or receivable	73	39

The record over five years of the cash value of the defined benefit rights, the fair value of the plan assets and the deficit of the benefit plan is as follows:

In thousands of Euro	2008	2007	2006	2005	2004
Cash value of the defined benefit rights	(357)	(165)	(305)	(164)	(110)
Fair value of the plan assets	208	111	179	93	55
Deficit	(149)	(54)	(126)	(71)	(55)
Adjustments based on experience: (increase)/decrease in pension obligations	(44)	(30)	(104)		
Adjustments based on experience: increase/(decrease) of the plan assets	(13)	(46)	43	(11)	(15)

We expect to contribute the sum of 149 K Euro to our defined-contribution benefit plan in 2009.

## 6.2.30. Subsidiaries

Name of the subsidiary	Place of incorporation and operation	Principal activity	
		2008	2007
ThromboGenics Inc.	US	100%	100%
ThromboGenics Ltd	Ireland	100%	100%

As part of simplifying the group structure, a cross-border merger between ThromboGenics NV and ThromboGenics Ltd is being studied.

### **6.2.31. Key agreements, commitments and contingent liabilities**

#### **Collaboration agreements on research and development**

The Group has entered into a number of research and development agreements with independent parties. In some cases these agreements include a cost-sharing plan for the project as well as the sharing of any revenue between the parties, so as to be able to defray the cost of commercializing the results of the project.

Please find below an explanation of our most important agreements. We consider an agreement as important when the commitments reach over 1 million Euro.

The main agreements are set out below.

#### **Research agreement with Chiltern**

In 2008, a research agreement was signed with Chiltern for two placebo controlled studies, of which one study will be executed in the US and the other in Europe and North-America. It is expected that in both studies a total of approximately 640 patients will be recruited. Both studies relate to Phase III microplasmin. The total fees for these studies are up to USD 12,596,616 for Chiltern Inc. and 8,525,038 Euro for Chiltern Ltd. In total, there are already 237,160 USD and 297,505 Euro recorded as intangible assets.

#### **Production agreement with Avecia**

In 2008, ThromboGenics concluded an agreement with Avecia for the production of microplasmin samples for a total value of 6,354,000 GBP. This contract relates to the Phase III clinical studies of microplasmin. Avecia is responsible for the production process for future commercial purposes. For this agreement, an amount of 1,323,084 GBP is recorded as intangible assets.

#### **License agreement with Selexis**

In August 2008 ThromboGenics signed an agreement with Selexis for the development of specific cell lines relating to the Anti-VPAC project. If the development proceeds according to plan, milestone payments will total up to 1 million Euro.

#### **Collaboration agreement in research and licenses with F. Hoffmann La Roche AG**

In June 2008, ThromboGenics and its partner BioInvent have granted a worldwide exclusive license to F. Hoffmann La Roche AG for the development and commercialisation of their jointly developed antibody TB-403. TB-403 is a humanized monoclonal antibody against PlGF (placental growth factor), a naturally occurring protein which promotes the formation of blood vessels.

ThromboGenics and BioInvent have formed, in collaboration with F. Hoffmann La Roche AG, a "Joint Steering Committee" to coordinate the research and development activities. ThromboGenics and BioInvent will retain the co-promotion rights for this product in the Benelux, Baltic and Scandinavian regions.

The potential cash value of this agreement amounts to 500 million Euro in milestone payments. ThromboGenics, which

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discovered TB-403, will receive 60% and BioInvent 40% of the income from the agreement with F. Hoffmann La Roche AG. In addition, double-digit royalties will be paid. In 2008, a non-refundable upfront payment of 50 million Euro has been transferred, of which ThromboGenics has received 30 million Euro as its share.

Third parties filed an objection with the European Patent Office regarding the patent rights in Europe. ThromboGenics has successfully defended the patent rights in a first phase, with virtually all patent claims retained by the European Patent Office. However, the third parties do have a right to a potential appeal. If the third party appeal were to be successful and the European patent was rejected, then royalties in Europe would be cut. If ThromboGenics were required to share the patent rights, then there will be no impact on the current earnings but only on the future earnings.

### **Collaboration agreements on research and licenses with BioInvent**

In September 2004, ThromboGenics Ltd and BioInvent International AB entered into an agreement to cooperate on research and licenses to develop together drugs based on antibodies for vascular disorders. The partners are developing two candidates together:

- Anti-Factor VIII (TB-402) as an anti-coagulation treatment for various indications such as the prevention and treatment of deep vein thrombosis and the treatment of atrial fibrillation; and
- Anti-PIGF (TB-403) as an anti-angiogenic component for the possible treatment of various disorders such as cancer, age-related macular degeneration, retinopathy and inflammation.

Under the terms of the collaboration the parties share the costs equally. When a candidate has been identified prior to the collaboration, the income is divided up on the basis of a 60/40 key (if a drug candidate is discovered during the collaboration, the income is divided up on the basis of a 50/50 key). For Anti-Factor VIII (TB-402) and Anti-PIGF (TB-403), ThromboGenics identified both drug candidates before the cooperation began and will therefore receive 60% of any future income.

### **Cooperation agreement with Geymonat**

In February 2004, ThromboGenics Ltd and Geymonat SpA entered into a cooperation agreement for the joint development of PIGF (Placental Growth Factor) as a pro-angiogenic growth factor that in pre-clinical studies appears to offer potential for the treatment of disorders such as ischemic heart disease.

Under the terms of the cooperation agreement, the parties share the costs equally. The income is shared on a 50/50 basis once the initial costs have been recouped. The agreement was initially concluded for a period of two years, but this has been extended by mutual consent. To date, no payments have been made under this agreement.

### **License agreement with NuVue Technologies**

In March 2004 ThromboGenics and NuVue Technologies Inc entered into a license and cooperation agreement for the development of plasmin-based products. ThromboGenics obtained an exclusive license for all current, pending and future intellectual property of NuVue Technologies Inc.

ThromboGenics has agreed to compensate NuVue Technologies Inc once a licensing agreement has been concluded with a third party. ThromboGenics could pay between USD 500,000 and USD 1,000,000 plus between 20% and 25% of the licensing income resulting from a third party agreement. To date, no payments have been made under this agreement.



If ThromboGenics were to commercialize microplasmin without a partner, the terms of the above deal can be renegotiated.

The company has concluded a number of agreements with various academic institutions that are interested in the study of drug candidates, including the following:

#### **Centrum voor Moleculaire en Vasculaire Biologie, KULeuven**

The Company has two cooperation agreements for projects under license from academic centres, namely the development of microplasmin, staphylokinase, Anti-Factor VIII and Anti-VPAC.

#### **Vlaams Interuniversitair Instituut voor Biotechnologie (VIB)**

The Company has concluded agreements with the Vesalius Research Center (*formerly the Dept. of Transgene Technology and Gene Therapy*) a department of the VIB, relating to the pre-clinical characteristics of two of the programmes under license with this institute, i.e., Anti-PlGF and PlGF.

ThromboGenics must pay to the VIB 15% of the license revenue received from third parties for the outlicensing of Anti-PlGF. Of this payment, 40% is borne by BioInvent. VIB shares 50% of this revenue with LSRP. In 2008, 4.5 million Euro was transferred to the VIB, which is 15% of the upfront payment (30 million Euro) received from Roche. The 4.5 million Euro is covered 40% by BioInvent (1.8 million Euro). The actual cost for ThromboGenics NV was 2.7 million Euro. (see note 2.8).

#### **Bharat Biotech**

In December 2006 ThromboGenics concluded a license agreement with the Indian company Bharat Biotech. Under the terms of this agreement, Bharat Biotech will bear all further development and commercialization costs relating to THR-100 (staphylokinase). ThromboGenics will receive double-digit royalties on future sales of this product.

#### **Rhein Minapharm Biogenetics**

In October 2007 ThromboGenics and Rhein Minapharm Biogenetics concluded a contract relating to the further clinical development and commercialization of THR-174 (staphylokinase), a derivative of the staphylokinase product. Rhein Minapharm will bear the further development and commercialization costs for this product, and ThromboGenics will receive milestone payments and double-digit royalties on future sales of this product. In 2007, ThromboGenics received an upfront payment of USD 200,000.

#### **Millipore**

In April 2007 ThromboGenics concluded a license agreement for the commercialization of its proprietary stem cell medium. As these activities no longer fall within the core programmes, ThromboGenics opted to outlicense this product. In 2007, an upfront payment was received for USD 60,000. In 2008, ThromboGenics also received two milestone payments totalling USD 100,000. In addition to milestone payments, ThromboGenics expects to receive double digit royalties in the future.

## The Group as a lessee in operational leases

On the balance sheet date the Group had outstanding commitments for future minimum lease payments, payable as follows:

In thousands of Euros (year ended op 31 December)	2008	2007
Less than one year:	347	164
More than one year but less than 5 years:	460	311
<b>Total</b>	<b>807</b>	<b>475</b>

ThromboGenics Ltd has concluded an operational lease relating to a building involving an annual commitment of 41,900 Euro until 2012, the earliest cancellation date, with the lease reviewed every five years.

In 2008 ThromboGenics NV concluded a new operational lease relating to a building involving an annual commitment of 225,000 Euro until 30 June 2017, the earliest cancellation date, although the lease can be terminated without costs every 3 years by ThromboGenics NV. The commitment has started on 01.07.08 for 25% (1 module) of the concerned surface. The other 75% (3 modules) will be leased as of beginning 2009.

ThromboGenics Inc. has concluded an operational lease relating to a building involving a commitment of 49,148 Euro for one year.

## Other commitments

### • Research and development commitments

As at 31 December 2008 the Group had commitments outstanding in the context of research and development agreements amounting to 30,989,958 Euro (2007: 5,991,707 Euro) payable over the course of the following 12 months to various research subcontractors.

### • Contingent liability

The expenses incurred in several of the Group's research and development programmes have been reimbursed by IWT or the EU, as a government grant. Contracts with IWT and the EU generally include a clause that defines the need for validation of the project results in order for the grant to be effectively earned. Should this validation not occur, IWT or the EU have the right to reclaim the funds previously granted. ThromboGenics NV Group considers this as a remote possibility. Total amounts received with respect to government grants from IWT and the European Union amount to 344,098 Euro (2007: 968,483 Euro).

## 6.2.32. Transactions with related parties

1. In September 2006, ThromboGenics NV has signed a lease with the Life Sciences Research Partners VZW (LSRP). This lease was in 2008 in mutual agreement ended on December 31, 2008.

In 2008, a total of 59,325 Euro has been charged. The last 2 quarters was 75% of the rent charge.

2. In May 2007, ThromboGenics decided to outlicense the antibodies against platelets glycoprotein Ib (anti-GP1b) and von Willebrand Factor (anti-vWF) to LSRP VZW in exchange for the sum of 1,100,000 Euro and a 25 % share in the future income that LSRP may receive for this programme.

3. ThromboGenics has patent, licensing and cooperation agreements on research completed by certain shareholders as Désiré Collen and third parties such as the VIB (Flanders Interuniversity Institute for Biotechnology). In 2008 there were 4,500,000 Euro paid to the VIB in the context of the F. Hoffmann La Roche AG Agreement. VIB shares 50% of this revenue with LSRP.
4. Désiré Collen, Chris Buyse and Patrik De Haes were remunerated by means of a management agreement between ThromboGenics NV and respectively Patcobel NV (a company in which Désiré Collen is a director), Sofia BVBA (a company in which Chris Buyse is a director) and ViBio BVBA (a company in which Patrik De Haes is a director). In the context of their consultancy agreements, the ThromboGenics Group paid out a total of 709,153 Euro in 2008 and 476,738 Euro in 2007.
5. For the non-executive directors a total amount of 79,000 Euro was recorded as charges in 2008 and 74,000 Euro in 2007, in the context of the exercising of their directors' mandates.

### 6.2.33. Remuneration of key management personnel

Remuneration of key management personnel was as follows:

Key management (in thousands of Euro)	2008	2007
Consultancy fees and reimbursement of expenses, short term	757	504
# of warrants and shares offered during the period (in thousands)	175	42
Consultancy fees in the long term in case of dismissal		
Minimum fee	474	410
Maximum fee	711	615

No loans, quasi-loans or other guarantees have been given to any of the executive directors.

Transactions with non-executive directors

Non-executive directors (in thousands of Euro)	2008	2007
Short-term employee benefits	79	74
<b>Total benefits</b>	<b>79</b>	<b>74</b>
# of warrants and shares offered during the period (in thousands)	-	-

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## **6.2.34. Financial instruments**

### **Use of derivative instruments**

On 31 December 2008, there were no outstanding derivative instruments.

### **Fair values**

There is no significant difference between the fair value and carrying amount of the Group's cash and cash equivalents, investments, trade and other receivables, other current assets, trade payables and other current liabilities.

The carrying amount of cash and cash equivalents and investments is equal to their fair value, given the short-term maturity of these financial instruments. Similarly, the historical cost carrying amounts of receivables and payables, which are all subject to normal trade credit terms, is equivalent to their fair values.

The assets available for sale are valued at fair value. The fair value adjustments are recorded in other reserves.

## **6.2.35. Events after the balance sheet date**

The following major events after the end of the year have been made for:

On February 20, 2009, both the Board of ThromboGenics NV and the Board of Directors of the ThromboGenics Ltd have approved "the joint merger proposal for a cross-border merger by acquisition related transaction". The relevant documents were already filed and will be submitted to shareholders for approval on 9 and April 30, 2009. This operation will undoubtedly simplify the structures and bring significant cost savings. They will have no impact on the operational activities of the Group.

On February 24, 2009 ThromboGenics was informed of a financial grant amounting to 3,221,364 Euro granted by the IWT, in the context of the further development of the Anti-VPAC1 program.

**Fees to the auditor**

	2008	2007
Remuneration of the auditor (s) for the exercise of an office of Commissioner at the level of the group of the company which publishes the information to the head	107,000	82,000
Remuneration for exceptional services or special assignments to this group by the Commissioner (s)		
Other audit assignments.	16,800	21,800
Tax Assignments	-	
Other assignments outside audit assignments	-	
Remuneration of the persons with whom the auditor (s) connected (s) for the exercise of an office of Commissioner at the level of the group of the company which publishes the information to the head	28,325	27,500
Remuneration for exceptional services or special assignments to this group of persons with whom the auditor (s) connected (s)		
Other audit assignments	-	
Tax Assignments	-	
Other assignments outside audit assignments	-	

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## 6.3. Annual Report of the board of directors on the consolidated annual accounts

Dear Shareholder,

We are pleased to present the consolidated financial statements as at 31 December 2008

### 6.3.1. Comments and approval of the consolidated financial statements 2008

The consolidated financial statements were prepared in accordance with IFRS and were approved by the Board of Directors on 12 March 2009.

ThromboGenics NV was incorporated on 30 May 2006 with a capital of EUR 62,000 represented by 11,124 shares. Per 31 December 2007 the capital of the company amounted to 114,772,856.20 EUR represented by 25,502,160 shares. During 2008 there were two capital increases:

- On 8 April 2008, warrants were exercised which resulted in a capital raise of 776,919.43 EUR and a capital premium of 86,225.57 EUR. In this capital increase 172,629 shares were issued.
- On 10 October 2008, 56,000 warrants were exercised and converted into shares, which resulted in a total of 25,730,789 shares. The capital was raised to 252,028.85 EUR of 776,919.43 EUR and a capital premium of 103,171.15 EUR.

Per 31 December 2008 the Company had a corporate capital of 115,801,804.48 EUR represented by 25,730,789 shares.

#### Profit- and loss account:

ThromboGenics generates revenue from license income. In June 2008 ThromboGenics announced a license agreement with pharma group F. Hoffmann La Roche AG.

F. Hoffmann La Roche AG received a worldwide and exclusive license to develop and commercialize TB-403, an anti-cancer antibody. Under the terms of this agreement, ThromboGenics received an upfront payment of 30,000 Euro. In accordance with IFRS this amount was recognized as revenue. The total revenues over the year 2008 amounted to 30,421 Keuro compared with 1,503 Keuro in 2007.

The other research programs and in particular the clinical programs booked considerable progress in 2008. The R&D expenses decreased from 17,232 kEuro in 2007 to 15,712 kEuro in 2008. The main part of these expenses are linked to the clinical programs.

The G&A expenses increased to 3,031 kEuro in 2008 compared with 2,315 kEuro in 2007. This increase is mainly due to the reinforcement of the team (a.o. HR, IT and administrative support) and an increase in consultancy fees.

In 2008 the Group generated a positive operating result of 10,587 kEUR compared with a negative operating result of 17,417 kEuro a year before.

Financial income in 2008 increased from 1,780 kEuro in 2007 to 3,348 kEuro, mainly due to the increased cash position on which interest was generated. Financial expenses also increased from 321 kEuro in 2007 to 1,750 kEuro and this mainly due to exchange rate differences.

The net loss of 15,967 kEuro in 2007 was converted to a profit of 12,095 kEuro in 2008.

**Cash Flow:**

The company operations generated a positive cash flow of 11,957 kEuro in 2008 compared with a cash drain of 14,797 kEuro in 2007.

The investing activities generated a negative cash flow of 22,486 kEuro in 2008 compared with 5,260 kEuro in 2007 due to an increase of investments. The investments relate to deposits with capital guarantee and terms between 3 and 6 months.

The net revenue from the issuing of shares amounted in 2008 and 2007 respectively to 1,249 kEuro and 28,251 kEuro. These funds raised in 2008 are due to capital raises by exercising of warrants.

ThromboGenics' position of cash and cash equivalents per end of 2008 amounted to 30,356 kEuro completed with 28,565 kEuro in cash deposits. In total ThromboGenics has a cash position of 58,921 kEuro to finance its future activities.

**Consolidated balance sheet:**

Due to the net profit of 12,095 kEuro realised in 2008 its equity was reinforced from 48,435 kEuro end 2007 to 62,393 kEuro per 31 December 2008.

The total balance sheet per 31 December 2008 amounted to 67,203 kEuro of which 88% cash and cash equivalents. The Group has no external financial debts. This comfortable position enables ThromboGenics to fulfill its financial commitments and to continue all the research programs.

**Commitments:**

ThromboGenics' commitments are exclusively related to operational lease commitments:

- As of 1 July 2008 ThromboGenics rents its labs and offices from NV Bio Incubator. The yearly rent amounts to 224,000 Euro. The rental agreement expires 30 June 2017 but can be renewed tacitly.
- The rent of offices in Dublin (Ireland) and New York (U.S.A) with an annual cost of respectively KEUR 42 and KEUR 47 yearly. The Irish rental contract can be terminated only as from 2012.

**Taxes:**

The Group has paid no taxes due to the retained losses in the previous financial year, with the exception of its subsidiaries in the US. Due to the unstable future profitability on a short term, ThromboGenics has no tax provisions booked on the balance sheet.

**6.3.2. Capital raises and issuing of financial instruments**

See above.

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### 6.3.3. Risks

In adherence to the Belgian company law, ThromboGenics has decided to inform the shareholders of the risks associated with the company. In 2008, ThromboGenics potentially was subject to the following risks:

- It takes a long time before a candidate drug is on the market. The preclinical and clinical studies are expensive and require a lot of time. Moreover, the outcome of each Phase is always uncertain.
- The government guidelines and rules are very strict and limited predictable.
- ThromboGenics is largely dependent on partners to generate revenue in the short or medium term, and to ensure expertise on production, sales, marketing, technology and license and property rights in the longer term.
- The inclusion of patients in clinical trials is complex and can have a negative impact on the timing and results of clinical trials.
- It is possible that ThromboGenics is unable to obtain a license for new candidate drugs.
- It is possible that the market is not ready for the candidate drugs of ThromboGenics.
- The pharmaceutical market is highly competitive.
- ThromboGenics may be exposed to violations of patents or other intellectual property rights.
- ThromboGenics may face difficulties in attracting good qualified staff.
- ThromboGenics has no background of operational profitability due to the substantial spending on research and development.
- It is possible that ThromboGenics will need additional financial investments to provide for his future activities.

In 2008, financial risk management focused on

- Credit risks

Since ThromboGenics does not have commercial activities yet, there is no credit risk at present.

- Interest risks

The Group does not have any financial debts and as such does not have important interest risks.

- Currency risks

To a limited extent, ThromboGenics is subject to exchange rate risks and will systematically match incoming foreign currencies (USD and GBP) with outgoing foreign currencies. In 2008, ThromboGenics has not used financial instruments to cover such risks.



### 6.3.4. Events after the end of the financial year

The following major events after the end of the year have been made for:

- On February 20, 2009, both the Board of ThromboGenics NV and the Board of Directors of the ThromboGenics Ltd have approved "the joint merger proposal for a cross-border merger by acquisition related transaction".
- The relevant documents were already filed and will be submitted to shareholders for approval on 9 and April 30, 2009. This operation will undoubtedly simplify the structures and bring significant cost savings. They will have no impact on the operational activities of the Group.
- On February 24, 2009 ThromboGenics was informed of a financial grant amounting to 3,221,364 Euro granted by the IWT, in the context of the further development of the Anti-VPAC1 program.

### 6.3.5. Provisions that may be triggered in the event of a public takeover on the Company (article 34 of the Royal Decree of 14 November 2007)

#### a. The powers of the Board of Directors with respect to the authorised share capital

Article 47 of the Company's articles of association contains the following provisions with respect to the authorised share capital. The powers of the Board of Directors with respect to the authorised share capital were renewed at the extraordinary shareholders' meeting on 26 May 2008. The Board of Directors has not yet used its powers with respect to the authorised share capital and thus the authorised share capital still amounts to 115,549,775.63 Euro.

"The board of directors is authorised, for a period of five (5) years from the publication in the Annexes to the Belgian Official Gazette of the deed of amendment to the articles of association dated 26 May 2008, to increase the share capital once or several times provided the cumulative amount of the increases does not exceed one hundred and fifteen million five hundred and forty nine thousand seven hundred and seventy five euro and sixty three cent (115,549,775.63 Euro). This authorisation to the board of directors may be renewed.

If the capital is increased within the limits of the authorised capital, the board of directors will be authorised to request payment of an issue premium. If the board of directors so resolves, this issue premium will be booked as a distinct fund, which may only be limited or removed by a resolution taken at a shareholders' meeting in accordance with the provisions on amendments to the articles of association.

The board of directors is authorised to amend the company's articles of association to record any capital increase decided on within the limits of the authorised capital.

This board of directors' authorisation will be valid for capital increases subscribed for in cash or in kind through the capitalisation of reserve funds, with or without issuing new shares. The board of directors is authorised to issue convertible bonds or warrants within the limits of the authorised capital.

The board of directors is authorised, within the limits of the authorised capital, to limit or declare inapplicable the preferential subscription rights granted by law to the holders of existing shares if in so doing it is acting in the best interests of the company and in accordance with article 596 onwards of the Belgian Company Code. The board of directors is authorised to limit or declare inapplicable the preferential subscription rights to the benefit of one or more persons, even if the affected persons are not members of the personnel of the company or its subsidiary.

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If the securities issued by the company are subject to a takeover bid, the board of directors may use the technique of the authorised capital to defend the company against this takeover bid, if it receives the notice sent by the Belgian Banking, Finance and Insurance Commission within a period of three years as of 26 May 2008 and insofar as (a) the shares issued as a result of the capital increase are as of their issue date paid-up in full, (b) the issue price of the shares issued as a result of the capital increase is not less than the price of the takeover bid and (c) the number of shares issued as a result of the capital increase is not more than one tenth of the capital shares issued prior to the capital increase.”

#### **b. The powers of the Board of Directors with respect to the purchase of own shares**

Article 48 of the articles of association of the Company contains the following provisions with respect to the purchase of own shares:

“To acquire its own shares by purchase or exchange, either directly or through a person acting in its own name but on behalf of the company, the company must comply with the formalities and conditions in articles 620 to 625 of the Belgian Company Code.

The board of directors is authorised under article 620 of the Belgian Company Code to acquire and hold shares if that acquisition is necessary to prevent an imminent and serious prejudice to the company. This authorisation is valid for three years from publication of the deed of amendment to the articles of association dated 26 May 2008 in the Annexes to the Belgian Official Gazette.

The board of directors is authorised under article 620 of the Belgian Company Code to acquire a maximum number of own shares that in the aggregate represents no more than ten percent (10%) of the issued capital, at a price which must be higher than ninety percent (90%), but lower than one hundred and fifteen percent (115%) of the price at which such shares were quoted on the stock exchange on the day preceding the day of the purchase or exchange. This authorisation will be valid for 18 months from publication of the deed of amendment to the articles of association dated 26 May 2008 in the Annexes to the Belgian Official Gazette. The authorisation is also valid for the acquisition of shares in the company by one of its directly controlled subsidiaries pursuant to article 627 of the Belgian Company Code.

The board of directors is authorised to sell all the company’s shares, at a price it determines, on a regulated stock exchange or in the framework of its remuneration policy to employees, directors or consultants of the company. This authorisation is valid without any time restriction. The authorisation is also valid for sales of the company’s shares by one of its directly controlled subsidiaries, as defined in article 627 of the Belgian Company Code.”

#### **c. “Change of control” provision with respect to warrants issued by the Company**

On 7 June 2006, the Company issued 500,000 warrants under the Warrant Plan 2006, 394,000 of which have been allotted, 24,000 of which have expired and 76,000 of which have been exercised. Consequently, at present, 294,000 warrants under the Warrant Plan 2006 have been allotted and are still exercisable and 106,000 warrants remain to be offered by the Board of Directors.

On 26 May 2008, the Company’s extraordinary shareholders’ meeting decided to issue an additional 450,000 warrants under the Warrant Plan 2008, 360,667 of which have been allotted, though are not yet exercisable. The remaining 89,333 warrants issued under the Warrant Plan 2008 remain to be offered by the Board of Directors.

On 26 May 2008, the Company’s extraordinary shareholders’ meeting approved, in accordance with article 556 BCC, the following “change of control” provision that was then included in the individual warrant agreements entered into between the Company and the individual warrant holders under the Warrant Plan 2006:

"If the Company becomes subject to a public takeover bid, the Warrants will also be exercisable during a period of fourteen calendar days following the formal notification of the public takeover bid by the Banking, Finance and Insurance Commission."

The Warrant Plan 2008 contains the following "change of control" provision in the event of a public takeover on the Company:

"If the company becomes subject to a public takeover bid, the allocated Warrants will immediately vest and will be exercisable during an exercise period of fourteen calendar days following the formal notification to the Company of the public takeover bid by the Banking, Finance and Insurance Commission."

### **6.3.6. The law of the 17 December 2008 concerning audit committees**

The Board of Directors confirms that, with regard to the Audit committees the Group complies with the new Law of 17 December 2008. De Audit Committee of ThromboGenics consists of non-executive directors of which at least one member has the necessary accounting and audit expertise

### **6.3.7. R&D**

Given the activities of ThromboGenics, the cost of R&D is very important. They represent more than 71% of total operating costs for the year 2008 compared with 86% in 2007. These costs mainly consist of costs for clinical trials paid to third parties and personnel costs.

Done on 12 March 2009,

On behalf of the Board of Directors.

## **6.4. Report of the statutory auditor on the consolidated annual accounts**

The auditor's report of KPMG Bedrijfsrevisoren represented by Michel Lange, dated 16 April 2009 contains the following opinion on the consolidated financial statements for the year ended 31 December 2008.

In our opinion the consolidated financial statements give a true and fair view of the Group's net worth and financial position as of 31 December 2008 and of its results and cash flows for the year then ended, in accordance with International Financial Reporting Standards, as adopted by the European Union, and with a legal and regulatory requirements applicable in Belgium.

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## 7. Glossary

Acute myocardial infarction (AMI)	A heart attack that is in the process of occurring.
Age-related macular degeneration (AMD).	A degenerative condition of the macula (central retina) that is the most common cause of vision loss in those 50 or older, with the disease affecting more than 10 million Americans.
Angiogenesis	The process by which new blood vessels are formed. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor, a mechanism that is caused by the release of chemicals by the tumor and that foster tumor vascularization and expansion.
Angioplasty	A surgical technique that widens narrowed arteries, usually by a balloon that, when deflated, is threaded into the affected area, then inflated to expand the hole through which the blood flows through the artery. The full name for the procedure is percutaneous coronary intervention (PCI).
Anticoagulant	A substance that prevents the clotting of blood. Also called blood thinner.
Antiplatelet	A substance that prevents blood platelets from clotting, thereby preventing blood clots.
Atrial Fibrillation (AF)	A disorder where the heart's atria (two small upper chambers) quiver instead of beating effectively. As a consequence, blood may pool and clot in the heart.
Clinical trial	A rigorously controlled test of a drug candidate or a new invasive medical device on humans.
Coronary Artery Bypass Graft (CABG)	A surgical technique in which areas of diseased arteries are removed and replaced by sections of healthy blood vessels from elsewhere in the body to help ensure an adequate supply of blood to the heart.
Coronary Artery Disease (CAD)	Narrowing and hardening (arteriosclerosis) of the coronary arteries that reduces the flow of blood to the heart muscle. These patients are at increased risk of developing a heart attack, also known as an acute myocardial infarction, or AMI (when clot forms over an unstable atherosclerotic plaque, severely blocking blood flow).
Coronary Heart Disease (CHD)	Synonymous with Coronary Artery Disease.
CMO	Contract Manufacturing Organization, or a company that is authorized by the drug authorities to produce material for administration to humans.
Critical Limb Ischemia (CLI)	Peripheral Arterial Occlusive Disease that has progressed to a stage in which there is not enough blood being delivered to the leg to keep the leg tissue alive. Evidence of CLI includes worsening pain, non-healing wounds, and gangrene.
Deep Vein Thrombosis (DVT)	A blood clot that forms in the larger veins of the body, most commonly in the leg. DVT is frequently a precursor of a pulmonary embolism. DVT and PE are commonly referred to as VTE.
Diabetic Retinopathy (DR)	A complication of diabetes caused by damage to the tiny blood vessels inside the retina, the light-sensitive tissue at the back of the eye. Diabetic retinopathy is the leading cause of blindness in the working-age population.

Embolic stroke	An ischemic stroke in which a clot forms, sometimes outside the brain, a piece breaks off and is carried by the bloodstream to a different vessel in the brain where it becomes lodged and cuts off the blood supply to the brain.
Embolism	An embolism occurs when a blood clot breaks loose from its site of formation and travels through the vascular system to a more distal site where it obstructs blood flow.
EMA	European Agency for the Evaluation of Medicinal Products
Fab Fragment	The portion of an immunoglobulin molecule that binds the antigen.
FDA	U.S. Food and Drug Administration, the agency responsible for the drug approval process in the United States.
Good Laboratory Practice (GLP)	The purpose of the GLP quality guidelines is to ensure a quality product, guiding pharmaceutical product research and development, but also to present a codex for many of the activities off the critical path of drug development.
Good Manufacturing Practice (GMP)	GMP standards are a part of the guarantee of the pharmaceutical quality of the drug and guarantee that drugs are made up and controlled in a consistent fashion, according to standard of quality adapted to the considered use and in compliance with provisions on drugs.
	Bleeding.
Hemorrhage	Bleeding.
Hemorrhagic stroke (Cerebral hemorrhage)	A stroke caused by the rupturing of weakened blood vessels in the brain, which causes bleeding into the surrounding tissue. The blood accumulates and compresses the brain tissue, causing injury.
Idiopathic Thrombocytopenic Purpura (ITP)	An autoimmune disease in which the body makes antibodies against its own platelets, leading to low platelet counts (thrombocytopenia).
IFRS	International Financial Reporting Standards
IND	Investigational New Drug Application If a new company wants to test a new drug in human patients, an IND must be prepared and filed with the relevant authority to request authorization to begin human testing of the drug.
Ischemic heart disease	A term often used interchangeably with coronary artery disease or coronary heart disease, wherein narrowing and hardening (atherosclerosis) of the coronary arteries leads to inadequate blood flow to the heart muscle.
Ischemic retinopathy	Damage to the retina caused by inadequate blood flow in the retinal arteries.
KULeuven	Katholieke Universiteit Leuven
LMWH	Low Molecular Weight Heparin
Macular Edema	Swelling of the central part of the retina (macula) that is responsible for central vision. This can be caused by diabetic retinopathy, as well as other conditions.
Monoclonal Antibody (Mab)	An antibody produced in a laboratory from a single clone that recognizes only one antigen and used as a therapeutic molecule targeting antigens from diseased cells.
Myocardial Infarction (MI)	An area of dead or dying tissue in the heart muscle (myocardium) resulting from insufficient or absent blood flow. Synonymous with "heart attack".
Ophthalmology	The branch of medicine that deals with the diagnosis, prevention, and treatment of disorders of the eye.
Orphan Drug Designation	Special status afforded certain drug candidates with the potential to treat a rare disease or condition.

Peripheral Arterial Occlusive Disease (PAOD)	Also referred to as Peripheral Arterial Occlusion (PAO) or Peripheral Arterial Disease (PAD). A condition associated with poor blood circulation in the legs that can lead to amputation or death.
Placebo	A medically inert substance given in connection with a controlled, double blinded clinical study.
Placental Growth Factor (PlGF)	A specific protein found in the body that is involved in the stimulation of new blood vessel formation. Although a homologue to VEGF, PlGF binds only to VEGFR-1 (Flt-1) (unlike VEGF, which binds to VEGFR-1 and VEGFR-2).
Plasmin	A fibrin-digesting substance or enzyme.
Plasminogen	An inactive enzyme circulating in the blood which may be used to create plasmin.
Plasminogen activator	An enzyme that converts plasminogen into plasmin
Posterior Vitreous Detachment (PVD)	The process whereby the vitreous (jelly-like substance that fills the center of the eye) detaches, or peels off from the back of the eye, away from the retina.
Pre-clinical Trial	A laboratory test of a new drug candidate or a new invasive medical device on animals or cell cultures that is conducted to gather evidence justifying a clinical trial.
Retina	The light-sensitive tissue that is present on the innermost back wall of the eye.
Retinal Detachment	The coming loose of the retina from the underlying tissue.
Pulmonary Embolism (PE)	Pulmonary embolism occurs when a blood clot that has formed elsewhere in the human body dislodges from its site of formation and travels to the arterial blood supply of one of the lungs where it causes obstruction of blood flow. PE and DVT are commonly referred to collectively as VTE.
Staphylokinase	A protein derived from the bacteria Staphylococcus Aureus that when administered to patients can induce the dissolution of a blood clot by binding to plasminogen in the presence of a blood clot.
Stroke	A stroke occurs when an artery carrying oxygen and nutrients to the brain is either blocked by a blood clot or bursts.
Systemic administration	Systemic administration means that the drug goes throughout the body (usually carried in the bloodstream), and includes oral administration (by mouth) and intravenous administration (injection into the vein).
Thrombocytopenia	Low platelet concentration in the blood.
Thrombolysis	The dissolution (breaking up) of a blood clot (thrombus).
Thrombolytic	A pharmaceutical that can break up blood clots blocking the flow of blood to specific tissues.
Thrombopoiesis	The process of platelet formation in the bone marrow.
Thrombotic Disease	A disease resulting from the formation of a blood clot in an artery or vein that obstructs vascular blood flow in a certain part of the body, such as the brain, heart or lungs.
Thrombotic strokes	An ischemic stroke, which involves clots that form in the brain.
Thrombosis	The formation of a blood clot locally within a blood vessel.
Thrombus	A blood clot.

## Notes





## Notes

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