Innovative Therapies for Retinal Disorders: Developing Disease Modifying Treatments for Diabetic Eye Disease

Company & Investor Presentation – September, 2017
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ThromboGenics
- Novel treatments for retinal disorders, focus on diabetic eye disease

- Front runner in discovery of new science in retina, now focusing on novel therapies for diabetic eye disease

- Progressing multiple (4) late-stage preclinical and clinical pipeline projects targeting novel therapies for Diabetic Retinopathy (DR) and/or Diabetic Macular Edema (DME): ocriplasmin, anti-PLGF, Plasma Kallikrein inhibitor, Integrin Antagonist + undisclosed

- Pioneer of new drug class of pharmacological vitreolysis and 100% owner of JETREA® (ocriplasmin)
  - JETREA® first and only approved pharmacological treatment for sVMA/VMT (approved in +50 countries globally, with nearly 30,000 patients treated in 20 countries)

- +85% owner of Oncurious NV (VIB venture partner):
  - Pediatric Oncology (US clinical trial)
  - 5 Immuno-Oncology projects (pre-clinical) since 09/2017

- 75 - 80 employees globally, HQ in Leuven (BE), US office in Iselin, NJ

- Cash position: + €120 million

Recent key development

**ThromboGenics Regains Global Rights to JETREA® (ocriplasmin)**

*Leuven, Belgium, 18th September, 2017* – ThromboGenics NV (Euronext Brussels: THR), a biotechnology company developing novel treatments for retinal disorders, with a focus on diabetic eye disease, announced today that it will regain full global rights to JETREA® from Alcon, a Novartis company, based on a mutual agreement that the unique characteristics of JETREA make ThromboGenics a better fit for building a sustainable long-term niche business.

- ThromboGenics and Alcon/Novartis transition commitment for continued JETREA access to customers and patients
- ThromboGenics to receive €53.7 million from Novartis as part of the agreement
- Novartis to invest €10 million in ThromboGenics equity
- ThromboGenics – cash of over €120 million to invest in diabetic eye disease pipeline post Novartis investment
ThromboGenics value proposition today: the Core

**Drug Development**
4 Preclinical / Clinical Compounds
Additional in discovery

**Disease Modifying Treatments**
Tackling Unmet Medical Needs in Diabetic Retinopathy
- THR-409 – ocirplasmin
- THR-317 – anti-PIGF
- THR-149 – plasma kallikrein inh.
- THR-687 – integrin antagonist
  For NPDR/PDR
  with or without DME

- Cash position = +€120 million
- Expected 2018 -20 Newsflow
- Fully funded – 4 yr horizon
ThromboGenics value proposition today: the Core... and more

- 100% THR owned
- US is cash neutral (>2016)
- Ex-US in transition from NVS
- Target cash-neutral to contributing

- Cash position = +€120 million
- Expected 2018 -20 Newsflow
- Fully funded – 4 yr horizon

- + 85 % THR owned
- Fully funded 3 yr
- VIB leads I/O developments
- BiolInvent/NMTRC to lead TB-403 trial

Drug Development
4 Preclinical / Clinical Compounds
Additional in discovery

Disease Modifying Treatments
Tackling Unmet Medical Needs in Diabetic Retinopathy
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Global BU Commercial

Oncurious
PhI/II TB-403
5 I/O projects
(preclinical)
Why diabetic eye disease?
Diabetic retinopathy segment is forecast to grow twice as fast as the overall ophthalmic pharmaceuticals market

**Ophthalmic pharmaceuticals market**

- **$19.6 Bio**
- **$7.2 Bio**
- **$1.6 Bio**

**Retinal diseases market**

- **$33.0 Bio**

**DR & DME segments market**

- **$12.8 Bio**

**Worldwide sales estimates 2015**

**Worldwide sales forecasts 2023**

**Compound Annual Growth Rate 2015-2023**

- **6.8%**
- **9.3%**
- **16.1%**


** Incl. at least wet AMD, DR/DME, and RVO markets

Abbreviation(s): AMD, age-related macular degeneration; DR, diabetic retinopathy; DME, diabetic macular edema; RVO, retinal vein occlusion; CAGR, compound annual growth rate

More than **One** in **three (!)** people with diabetes will develop diabetic retinopathy

35.4%

**NPDR**
Non-proliferative diabetic retinopathy

**PDR**
Proliferative diabetic retinopathy

**with or without DME**
Diabetic macular edema
ThromboGenics is developing **novel therapies for all DR segments**

**ANY DR**

- **NPDR without DME**: 23.6%
- **NPDR with DME**: 4.5%
- **PDR without DME**: 4.2%
- **PDR with DME**: 3.0%

*Any DR is defined as the presence of NPDR, PDR, DME or any combination thereof*

Abbreviation(s): DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; DME, diabetic macular edema;

Source(s): Yau 2012; Int’l Diabetes Federation and the Fred Hollows Foundation 2015; National Eye Institute 2015
### Drug Development Targeting all DR segments: ‘*Multiple Shots on Goal!*’

#### Therapeutic action

<table>
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<th>PROGRAM</th>
<th>HALLMARKS OF DIABETIC RETINOPATHY</th>
<th>SEGMENT</th>
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<td></td>
<td>Inflammation</td>
<td>Edema</td>
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<td><strong>THR-409</strong> (ocriplasmin)</td>
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1. prevention blood vessel ingrowth in vitreous (PVD)
2. neo-angiogenesis inhibition + prevention blood vessel ingrowth in vitreous (PVD)

+ = level of therapeutic action
THR-409 : ocriplasmin
THR-409: Inducing a Total PVD with NPDR patients
(Ocriplasmin)

- THR-409 is a disease modifying compound
  - unique mode of action: Posterior vitreous detachment (PVD)

- Phase II CIRCLE study exploring multiple injection regimen
  - Patients: moderately to severe NPDR patients
  - Up to 3 injections of commercial dose / half dose arm
  - Revised protocol – access to broader patient pool

- Potential step-change in the disease management in NPDR:
  - Study will explore progression rates to PDR
  - No other medical products approved for this indication
THR-317 : anti-PIGF (Placental Growth Factor)
THR-317: Placental growth factor (PIGF) is an optimal target to treat more advanced stages in diabetic eye disease

Increasing levels of PIGF correlate with increasing levels of retinal ischemia

THR-317: Key take aways

- THR-317 is disease-modifying
  - DME, with potential additional benefit in anti-inflammatory treatment and fibrosis prevention
- Recruiting patients (n=50) in Phase I/IIa
- Only drug in development that targets solely PlGF
- THR-317 offers the potential for two treatment modalities
  - Stand-alone treatment in DME
  - Combination treatment with anti-VEGF
- Sizeable target population
- Phase I/IIa results anticipated Q1 2018
THR-687 : Integrin receptor antagonist
THR-687 Rationale: differential effects of inhibiting VEGF and integrin

Integrin antagonism provides multiple points of attack to treat diabetic retinopathy

Angiogenesis cycle
endothelial cell migration, proliferation, differentiation and maturation

TARGETING VEGF

TARGETING INTEGRIN

Integrin antagonism treats disease root cause (vascularization) with multiple points of attack

Adapted: Boyer 2014 The Ophthalmologist 38-40
THR-687: Key take aways

- THR-687 is a novel and potent integrin antagonist
- THR-687 has a broad therapeutic potential
  - diabetic retinopathy with and without DME
- NPDR / PDR indication
  - treatment of diabetic retinopathy
  - induction of total posterior vitreous detachment
- Sizeable target population
- Phase I/IIa study to be initiated H1 2018
THR-149 : a Plasma kallikrein (PKal) inhibitor
Plasma kallikrein & diabetic macular edema

**Preclinical evidence**
- PKal mediates vascular hyper-permeability, leukostasis, cytokine production, and retinal thickness
- PKal inhibition significantly inhibits retinal vascular leakage in a diabetic mouse model

**Clinical evidence**
- Upregulation of intraocular plasma kallikrein contributes to a VEGF independent mechanism
- Retinal expression of Bradykinin-1 receptor is increased
THR- 149 : Key take aways

- THR-149 is a potent and selective plasma kallikrein inhibitor

- THR-149 is targeting the treatment of diabetic macular edema (DME)
  - impact on disease on-set and progression

- THR-149 offers the potential for two treatment modalities
  - stand-alone therapy in diabetic retinopathy with DME
  - refractory DME to current treatment

- Sizeable target population

- Phase I/IIa study to be initiated H1 2018
Diabetic Eye Disease – pipeline / newsflow
Drug Development Targeting all DR segments: ‘Multiple Shots on Goal’ – different mechanisms of action
JETREA®
(ocriplasmin)
Intravitreal Injection, 2.5 mg/mL
JETREA® Commercial Update

- ThromboGenics regained global rights to JETREA® (non-US rights were with Alcon/Novartis until 16/09/2017)

- HY17 reported JETREA® revenue: €2.7m (incl €800k non-US royalties)

- JETREA in the US - break even:
  - Small team, specialized distribution partner, online resources for patient, physician information, including enrollment and reimbursement

- US Launch of new JETREA® ‘Already-Diluted’/ ‘Ready to Use’ formulation imminent

- JETREA® now approved in over 50 countries/ patients treated in 20 countries

- OASIS 2 year follow up data reporting better outcomes than Phase III trial results: confirming positive long-term efficacy and safety data (published in Ophthalmology – AAO Journal)

- Continued ocriplasmin data generation and dissemination: conference and publication plan 2017
Focused on cutting immuno-oncology assets
Recent Highlights

- Oncurious acquiring VIB portfolio of 5 next-generation immuno-oncology projects targeting a broad spectrum of cancers
- VIB increases shareholding in Oncurious
- Add-on to existing activities (clinical trail) in pediatric brain cancers
- ThromboGenics invests €2.1 million in Oncurious as part of this agreement
- ThromboGenics now owns +85% of Oncurious
Oncurious TB-403 Update

- Evaluating TB-403 for medulloblastoma
  - TB-403’s safety has previously been studied in 70 adult cancer patients (Lassen 2012, Martinsson-Niskanen 2011)
  - Compelling data on therapeutic action of TB-403 in medulloblastoma (Harvard)
- Phase I/II a has been initiated – development of TB-403 for medulloblastoma
  - Collaboration agreement has been signed with NMTRC to conduct the Phase I/II trial in the US
- BioInvent International is TB-403 development and business partner (50/50 – development cost and economic benefit)
- European Commission confirmed orphan drug designation for TB-403 for medulloblastoma following a positive opinion issued by the European Medicine Agency (EMA) – January 2017
Summary & key take aways
ThromboGenics
- Novel treatments for retinal disorders, focus on diabetic eye disease

- Progressing multiple (4) late-stage preclinical and clinical pipeline projects targeting novel therapies for Diabetic Retinopathy (DR) and/or Diabetic Macular Edema (DME): ocriplasmin, anti-PLGF, Plasma Kallikrein inhibitor, Integrin Antagonist + undisclosed

- Significant pipeline newsflow over the next 12 months

- Pioneer of new drug class of pharmacological vitreolysis and 100% owner of JETREA® (ocriplasmin)
  - JETREA® first and only approved pharmacological treatment for sVMA/VMT (approved in +50 countries globally, with nearly 30,000 patients treated in 20 countries)

- +85% owner of Oncurious NV (VIB venture partner): ongoing clinical trial + 5 next gen I/O projects

- Over €120 million in cash to invest in pipeline development

- Welcoming Novartis AG as a shareholder (€10m investment)

- Experienced management team focused on delivering value generating milestones
Thank you for your interest

For questions and information:
Please send your message at IR@thrombogenics.com