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Unflagging efforts to prevent vision loss worldwide

Less than a year after launching four new clinical trials, Oxurion is accelerating its drug development pipeline and is on track to publish initial data later in 2019. In 2018 major milestones were met and the company renamed, but CEO Patrik De Haes and Chairman Thomas Clay predict the true excitement will come as the first results of these efforts become visible.
"We look at 2018-2019 as one timeframe with two parts," explains CEO Patrik De Haes. "In 2018 we changed our name and brand, but more importantly we defined our strategic ambitions: to start the four clinical trials and set up a fully operational business unit for Jetrea after acquiring the global rights from Novartis. We hope to see these efforts starting to pay off by the end of 2019."

Chairman Thomas Clay concurs. "The agreement with Novartis at the end of 2017 indeed produced a two-year plan. The transaction gave us back Jetrea, a first-in-class product, and the cash infusion enabled us to invest strongly in our development pipeline in 2018. Over the next year these investments will generate first data and we hope to see the positive impact of commercializing Jetrea on our business soon after."

With THR-317, an anti-PIGF, Oxurion is currently evaluating its efficacy and safety when administered in combination with an anti-VEGF (Lucentis®) to treat diabetic macular edema (DME). Research shows that this could offer an improved treatment option for patients who don’t respond well to anti-VEGF mono-therapy.

DME is a complication of diabetic retinopathy (DR) that causes an accumulation of fluid and swelling in the macula, resulting in vision loss. "We also started a second Phase 2 clinical study with THR-317 to evaluate it for treatment of idiopathic macular telangiectasia type 1 (MacTel1), a rare degenerative retinal disease for which there is currently no therapy."

In May 2018, Oxurion initiated a Phase 1 clinical study evaluating the safety of THR-149, a plasma kallikrein inhibitor, to treat patients with DME. "This is a validated pathway and a different angle to attack the disease," explains Patrik De Haes. A fourth clinical trial has been launched evaluating the safety of THR-687, a pan-RGD integrin antagonist, to preserve vision in a broad range of patients with diabetic eye disease. "This is yet another path to finding a novel treatment for diabetic eye disease, with a compound offering a very broad potential."

Chairman Thomas Clay says the multi-pronged approach makes the Oxurion pipeline very interesting to investors. "It’s a way to offer a portfolio with reduced risk. We don’t just rely on one technology or molecule, and we are targeting pathways validated by the development programs of several competitor companies."

"Our current value and position as a global biotech player are the fruit of proven past R&D efforts that led to sustainable research models."

Thomas Clay, Chairman of the Board of Directors

Strong progress of clinical development pipeline

This past year Oxurion invested heavily in advancing its pipeline targeting back of the eye diseases, starting four clinical trials with three molecules. "That was quite an achievement, and we owe it to the tireless work of the whole clinical development team. It was intensive, but based on patient recruitment to date, we are confident in our ability to produce results for all those trials by the end of 2019," Patrik De Haes explains.
Sustained investment in R&D

Moreover, Oxurion continues to invest in discovery programs for new target diseases in the back of the eye. “It is critical to a biotechnology company to push R&D and constantly generate new concepts at the preclinical level. That way we can keep bringing new products into the clinic and add value to our portfolio,” explains Thomas Clay.

“Our current value and position as a global biotech player are the fruit of proven past R&D efforts that led to sustainable research models. Our decisions to invest in early stage compounds have already generated visible results: we brought a first-in-class product to the market and now have an exciting pipeline with three other products in clinical trials. The success factor in all these strategic considerations is good interaction between the Management Team and the Board of Directors.”

The company is now entering the field of age-related macular degeneration (AMD), one of the world’s leading causes of blindness in elderly people. In the ‘dry’ form of the disease (dry AMD), retinal tissue slowly wastes away due to cell degeneration. In its most advanced stage the condition leads to blindness. “We’ve partnered with Beta Therapeutics in a discovery program for this degenerative disease, while still keeping our focus on diabetic eye disease,” says Patrik De Haes.

“We hope to see all our efforts starting to pay off by the end of 2019.”

Patrik De Haes, MD, CEO

New name well received

2018 also saw the renaming and rebranding of the company, formerly known as ThromboGenics. The Chairman reports that the new Oxurion name has already taken firm root in the biotech landscape. “The previous name no longer reflected our focus on eye disease and our ambitions in that area. We started the strategic transformation several years ago but to the outside world the magnitude of the reset and its value were unclear. The new name Oxurion has been very well received.”

“The renaming is basically the final piece of a process we started a few years ago to redefine our company’s strategic focus,” Patrik De Haes adds.

Oncology research ongoing with Oncurious

While Oxurion is focused on the retinal space and more specifically diabetic eye diseases, its subsidiary company Oncurious, founded together with VIB (Flanders Institute for Biotechnology), is pursuing R&D work in oncology.

“The clinical trial of the antibody TB-403, an anti-PlGF, for treatment of medulloblastoma is progressing. Together with Beat Childhood Cancer, Oncurious is still recruiting patients for this study with the ultimate goal of curing this rare and very deadly brain tumor in children,” says Patrik De Haes. “Meanwhile, Oncurious is advancing its preclinical research with the portfolio of next-generation immuno-oncology assets acquired from VIB. We expect preclinical proof of concepts in the next two years.”
Strong organization and experienced Board of Directors

Over the years Oxurion has built a strong, agile and very complementary organization. CEO Patrik De Haes is proud of how long team members usually stay with the company. “The average time of an employee at Oxurion is over six years, which is very high in a biotech context. That proves we’re a stable firm.”

“Our preclinical team is really the driver of our R&D work to discover new pathways. To bring new compounds into the clinic and advance our pipeline, we have a very experienced clinical team with a proven track record in regulatory, quality and safety issues. Much new data will be generated in the coming year so we’re now bolstering our statistical analysis capabilities,” says Patrik De Haes.

As for the Board of Directors, Chairman Thomas Clay points to the replacement of Paul G. Howes by Adrienne Graves. “First, the company expresses its gratitude to Paul for many years of loyal service. The change was driven by multiple factors, one being our clinical focus. Adrienne’s background and her community network have already added value to our work. Also, One-third of the Board now consists of female executives. With 50% Europeans and 50% Americans, we’re proud to have a perfectly balanced team.”

Eye community

Over the past year Oxurion has increased its interaction with NGOs and patient organizations like Prevent Blindness and Retina Global. “The full Oxurion Board attended an event organized by Retina Global, since we’re a leading sponsor of a Bolivian project to train local physicians and nurses in diagnosing and treating diabetic retinopathy and eye diseases in general in a population that normally cannot afford it,” Patrik De Haes says.

“By supporting events like these we want to reach out to the broader eye community to join forces and show our dedication to fulfilling our mission: to prevent vision loss and fight blindness worldwide by developing and delivering next-generation treatments.”
Back of the eye disease: filling the gap

The World Health Organization says that 80% of vision impairment is avoidable. Some 1.3 billion people suffer from some form of vision loss, including 36 million who are blind. Even with staggering numbers like these we face a high unmet need in treating the leading cause of vision loss: back of the eye diseases, many of which are caused by diabetes. By joining forces with two dedicated nonprofit organizations - Prevent Blindness and Retina Global - Oxurion aspires to meet this urgent need in the near future.

Jeff Todd, CEO and President of Prevent Blindness and Rajat Agrawal, CEO of Retina Global

“Creating awareness and groundbreaking research go hand in hand”

Global rising life expectancy and population growth mean more people with severe back of the eye conditions caused by diabetes and ageing. Nonprofit organizations like Retina Global and Prevent Blindness state that boosting awareness is essential and should go hand in hand with groundbreaking research.

For diabetic retinopathy alone it is estimated that 93 million people worldwide have the disease. The same goes for age-related back of the eye diseases such as dry AMD. The 2.2 million AMD patients in the US, for instance, will double by 2050. *

Through partnerships with nonprofit organizations like Retina Global and Prevent Blindness, Oxurion strives to have an impact extending beyond the medical and scientific: to raise awareness, provide care in areas where it is needed most, and ultimately improve patients’ quality of life.

The patient’s voice

“The partnership between Oxurion and Prevent Blindness works so well because our missions align perfectly. We’re both passionate about enabling people to see the world through healthy eyes,” says Jeff Todd, President and CEO of Prevent Blindness.

“Oxurion plays a crucial part in that by conducting innovative research and developing medications to treat vision impairment. Prevent Blindness has a complementary role: educating the public, working to improve access for all to quality eye care, and making sure patients’ voices are heard through our national and state advocacy efforts.”

Rajat Agrawal, MD, CEO of Retina Global, agrees. "Oxurion is truly committed to providing care around the globe. Thanks to their support, we can treat patients and offer quality education to eye doctors in developing countries."

He's enthusiastic about the Oxurion clinical development pipeline and looks forward to more collaboration. "We're excited to see what the future brings so we can help even more patients. We must keep stressing the importance of routine retinal check-ups for risk groups."

"Thanks to partnerships between the research industry and nonprofit organizations we can have an impact that stretches far beyond the medical and the scientific."

Jeff Todd, CEO and President of Prevent Blindness and Rajat Agrawal, CEO of Retina Global

"In developing countries especially eye surgery is very expensive and time-consuming. Moreover, getting eye injections, such as with anti-VEGF to treat diabetic macular edema, is something many patients must be convinced of, whether for mental or practical reasons. Finding valuable alternatives or improved therapies could be a huge benefit."
Spreading the message

Finding novel treatments is one key aspect, but with retinal disorders prevention and awareness are just as powerful. Jeff Todd: “Many back of the eye diseases - such as dry AMD and diabetic retinopathy - cause no noticeable symptoms in early stages. By the time patients do notice them, irreversible vision loss has already been done and their lives may never be the same.”

“Thanks to Oxurion’s support we’re able to get our message about the importance of vision and eye health across in a powerful and efficient way, fully exploiting the resources and possibilities of both classic and social media. During Diabetic Eye Disease Awareness month in November 2018, for instance, we worked closely together to reach even more people to provide them with the information they need to protect vision.”

What are back of the eye diseases?

Back of the eye diseases (also known as retinal disorders) are conditions that affect the retina, a thin layer of tissue at the inner back of the eye. Examples include diabetic retinopathy, dry and wet AMD, and macular telangiectasia (or MacTel). Patients who suffer from these commonly don’t experience any symptoms in an early stage but start losing their vision later. The most common causes for these retinal diseases are diabetes and old age.*

Retinal disorders in numbers

- An estimated **1.3 billion** people live with some form of vision impairment, **36 million** are blind. **
- Chronic eye diseases are one of the main causes of vision loss globally, accounting for an estimated **90%** of visual impairment cases. A significant portion of disorders are conditions related to the back of the eye. ***
- Some **93 million adults worldwide** are affected with diabetic retinopathy, the leading cause of vision loss in the working population. ****
- In the **US alone, 2.2 million** people are visually impaired due to dry AMD. By 2050 this number will double to 4.4 million. *****

* Source World Health Organisation: www.who.int

** Source World Health Organisation, www.who.int

*** Source Research Report: Back of the Eye Disorders: Novel Drugs and Delivery Technologies, 2018-2030, Roots Analysis

**** Source DR Barometer, drbarometer.com

Retina Global and the BOLDR project

Nonprofit organization Retina Global treats and prevents blindness caused by retinal diseases in developing countries.

Supported by the World Diabetes Foundation and Oxurion, Retina Global has just launched BOLDR (Bolivian Diabetic Retinopathy), a project committed to providing retinal care and ophthalmological education in Bolivia. As in the rest of the world, diabetes and diabetic retinopathy are worsening problems in the country. Oxurion supports the project in achieving three valuable goals:

1. Educate eye doctors and other medical professionals: Retinal specialists give formal certification courses on recognizing, diagnosing and treating back of the eye diseases.

2. Provide care for patients who suffer from back of the eye diseases.

3. Raise awareness and reach out to the community, so risk groups such as the elderly or diabetics know about the need for routine eye check-ups and which treatments are available.

Prevent Blindness: getting the message across

Prevent Blindness provides information, resources, and technical assistance to prevent blindness and preserve sight in the US. The organization works to:

- increase awareness and educate people on the importance of taking care of their eyes;
- advocate for public policy and resources that ensure everyone has affordable, accessible, and quality eye care options, including preventive vision screenings, comprehensive eye exams and appropriate treatment, and low-vision devices;
- provide patient support through education and awareness campaigns, free/low-cost eye care assistance through industry partnerships, and programs that empower individuals living with vision challenges – and their caregivers;
- strengthen public health systems to provide a continuum of vision care for young children, through its National Center for Children’s Vision and Eye Health, by helping states strengthen screening protocols, improve access to exams and treatment, bolster capacity for surveillance, and develop success yardsticks;
- serve as a resource for public health professionals on areas related to eye health through an annual national eye health summit, webinars, allied health education, surveillance efforts, research grants, and professional recognition awards.
Back of the eye disease: filling the gap

Perspectives
Improved therapies for diabetic eye disease

Diabetic eye disease is a leading cause of blindness in people of working age worldwide. About half of these patients respond poorly or not at all to the current standard of care. Prevention and a healthy lifestyle are crucial to managing the condition in an early stage. Alternative treatments to combat the disease in several stages or enhance current therapies can greatly improve patients’ quality of life. Oxurion is developing a pipeline of disease-modifying drug candidates for diabetic eye disease.
With approximately 425 million adults worldwide living with diabetes, a number that will rise exponentially to 629 million in 2045, global healthcare is facing a pandemic. About 30% to 40% of this population will develop some form of diabetic eye disease and is at risk of going blind. “There is an urgent need to diagnose and treat patients in an early stage of the disease,” says Professor Sehnaz Karadeniz, MD, ophthalmologist and Regional Chair of the International Diabetes Federation Europe Region (IDF Europe).

Diabetic eye disease is currently the one of the leading causes of preventable blindness in the working population worldwide. “Unfortunately, the number of people with diabetes globally is still exponentially growing. Knowing that there are a lot of patients that even remain undiagnosed, it is not difficult to understand that the problem is huge,” explains Prof. Karadeniz.

“At IDF and IDF Europe, we embrace all efforts to tackle diabetes and related vision loss across the globe: innovative research, clinical trials but also initiatives to create more awareness. The pharma industry, biotech companies like Oxurion, patient advocacy organizations … we should all join forces to fight the problem.”

**Vision loss affects life quality**

Diabetic retinopathy (DR) is a common and most feared complication of diabetes, because it leads to vision loss and – in a severe stage – even blindness. The condition occurs when high blood sugar levels cause damage to blood vessels in the retina, causing them to swell and leak or even close. The disease affects roughly 145 million people globally. DR also can lead to diabetic macular edema (DME), which is caused by an accumulation of fluid in the macula due to leaking blood vessels. This condition also leads to progressive vision loss that greatly affects patients’ quality of life. “They have problems with everyday activities, like reading, driving the car, cooking or cleaning,” says Prof. Karadeniz.

Many of them only get diagnosed in a late and severe stage of the disease. A lot of people living with diabetes are not even aware that they have the disease. Related conditions like diabetic retinopathy develop gradually, so people with diabetes may initially not be aware of any changes in their vision. They only go to an ophthalmologist when their sight is already affected by diabetic eye disease. At that point, our primary target is to try to preserve their remaining vision,” she says.

Awareness

That is why it is essential, according to Prof. Karadeniz, to create more awareness about diabetes and the conditions related to it. “At IDF and in our Region we focus on promoting diabetes care, prevention and cure worldwide. There are a number of factors that influence the development of type 2 diabetes, related to lifestyle, physical activity and a healthy diet. That is why for example, we give recommendations for a healthy diet.”

“For people who get diagnosed with diabetes type 1 or type 2, it is crucial that we screen them on a regular basis to detect complications like diabetic retinopathy in an early stage.”

Improved therapies

The current standard of care to preserve vision in people with diabetic eye disease includes anti-VEGF injections or laser therapy besides good metabolic control. “Both are very effective, but the burden of treatment is quite high: with anti-VEGF for example, patients need to undergo repeated injections in the eye. Also, some people with diabetes may not respond good to this therapy so we need alternatives.”

“That is why we are closely monitoring all clinical trials and promising developments in that area. Novel therapies with improved efficacy or lowering the burden of treatment would certainly benefit people with diabetes.”

About Professor Sehnaz Karadeniz

For the past 20 years, ophthalmologist Sehnaz Karadeniz, MD, has been actively involved in the field of diabetes in a series of medical, scientific, and social projects at national and international levels. She teaches at the Ophthalmology Department of the Medical Faculty of Istanbul Science University and also works as an ophthalmologist at the Ophthalmology Dept. of the Istanbul Florence Nightingale Hospital.

She is IDF Europe Regional Chair and the Founding Member and Member of the Board of Trustees of the Turkish Diabetes Foundation (TURKDIAB) that was established in 1996. Since then, she has been actively involved in the social and scientific activities of the Foundation, and also has been voluntarily coordinating its international relations since 2003. In addition, she coordinates the DIABLIVA project of the Turkish Diabetes Foundation, an initiative that provides support for Turkish immigrants with diabetes. From 2004-2007, Dr. Karadeniz served as President of the Living with Diabetes Association, a nationwide patients’ organization, and from 2008-2014, as Board Member responsible for Association development.

She joined the board of the International Diabetes Federation European Region (IDF Europe) in 2007, and has been the Chair of the IDF European Region since December 2015. She is also an EASD Council Member for the 2014-2017 term.

(Source: https://www.idf.org/regional-chair.html)

“Many of them only get diagnosed in a late and severe stage of the disease. A lot of people living with diabetes are not even aware that they have the disease. Related conditions like diabetic retinopathy develop gradually, so people with diabetes may initially not be aware of any changes in their vision. They only go to an ophthalmologist when their sight is already affected by diabetic eye disease. At that point, our primary target is to try to preserve their remaining vision,” she says.

For people who get diagnosed with diabetes type 1 or type 2, it is crucial that we screen them on a regular basis to detect complications like diabetic retinopathy in an early stage.”
About the International Diabetes Federation and IDF Europe

The International Diabetes Federation (IDF) is an umbrella organization of over 240 national diabetes associations in 168 countries and territories. It represents the interests of the growing number of people with diabetes and those at risk. The Federation has been leading the global diabetes community since 1950. IDF’s mission is to promote diabetes care, prevention and a cure worldwide. IDF is engaged in action to tackle diabetes from the local to the global level - from programs at community level to worldwide awareness and advocacy initiatives.

The International Diabetes Federation is divided into seven regions, with the aim of strengthening the work of national diabetes associations and enhancing the collaboration between them. IDF Europe is the European chapter of IDF, representing 69 national diabetes organisations in 44 countries across Europe.

The Federation’s activities aim to influence policy, increase public awareness and encourage health improvement, promote the exchange of high-quality information about diabetes, and provide education for people with diabetes and their healthcare providers. IDF is associated with the Department of Public Information of the United Nations and is in official relations with the World Health Organization (WHO).
Diabetic retinopathy (DR)

There are two types of DR: non-proliferative (NPDR) and proliferative (PDR). NPDR occurs in an early stage, when microaneurysms and leaking blood vessels (hyperpermeability) cause inflammation in the back of the eye.

As NPDR progresses from moderate to severe the patient may develop PDR, characterized by an abnormal growth of blood vessels in the vitreous or along the retina’s surface that eventually causes permanent damage through development of scar tissue (fibrosis).

Diabetic retinopathy has a major impact on patients’ quality of life and their ability to perform daily activities such as driving a car, working, and performing household chores. DR can cause blurry or cloudy vision or make colors look faded. If left untreated, DR can lead to blindness.

Diabetic macular edema (DME)

DME is a complication of DR characterized by an accumulation of fluid in the macula. It can occur at any stage of the disease. The macula is responsible for sharp vision so swelling results in debilitating progressive vision loss that greatly affects patients’ quality of life (such as reading and driving).
Clinical development update

Oxurion accelerates drug developments for diabetic eye disease

This past year Oxurion has stepped up its clinical development efforts in diabetic eye disease. Three drug candidates are being evaluated to treat diabetic retinopathy or diabetic macular edema.

Roughly half of patients with diabetic retinopathy (DR) and diabetic macular edema (DME) respond not at all or not well to the current standard of care, conventional anti-VEGF therapy. Laser therapy is an alternative but both treatments are fairly intrusive: injections with anti-VEGFs must be repeated several times to ensure effectiveness.

Oxurion’s three drug candidates for diabetic eye disease are unique in their pharmacology compared to current options. By attacking the condition from distinct disease-modifying pathways, Oxurion hopes to meet the high medical need for novel therapies to improve patients’ outcome.

The anti-PIGF THR-317 can potentially target inflammation by reducing leakage of blood vessels and an increase in vessel maturation in an early stage of DR. This could change the disease’s progression and offer patients added benefits by improving the efficacy of care when used in combination with anti-VEGF therapy. The phase 1/2 clinical trial with this drug candidate showed it is safe, well-tolerated and showing an increase in vision in a certain percentage of patients with DME, like that observed with anti-VEGF therapy. Oxurion started a phase 2 clinical trial in 2018 and completed the recruitment of 70 patients to evaluate the efficacy of THR-317 in combination with Lucentis (ranibizumab), a conventional anti-VEGF, for treating DME.

THR-149, a plasma kallikrein (PKal) inhibitor, is a potential alternative option for DME patients who are poor- or non-responders to current treatments. The anti-edema activity of PKal pathway is validated in preclinical and clinical setting. PKal inhibition has also been reported to decrease micro aneurysms formation. It can potentially be used as a stand-alone treatment for poor responders to anti-VEGF therapies or in combination with it. The phase 1 clinical trial that Oxurion started this past year (in anti-VEGF naïve patients) is actively recruiting patients to assess its safety in those with central-involved diabetic macular edema.

THR-687, a novel pan-RGD integrin antagonist, has a broad therapeutic potential for DR and DME. The molecule targets multiple processes involved in DR and could offer benefits in both early and later stages of the disease. Oxurion has started a phase 1 clinical trial to assess the safety of the compound in patients with DME.
Preserving vision in an ageing population

People across the globe are living longer. By 2050, the world’s population aged 60 and older is projected to be 2 billion.* Health conditions associated with ageing will have a large impact on their lives and on healthcare systems. These include vision loss, mostly caused by cataracts or age-related macular degeneration. Oxurion is working to meet these challenges with novel research pathways.

Age-related macular degeneration (AMD) is a leading cause of blindness, especially in the Western countries. Studies show some 196 million people globally will likely be affected by AMD by 2020.* Most have the ‘dry’ form of the disease in which retinal tissue slowly wastes away due to cell degeneration. Dry AMD (sometimes known as atrophic AMD or geographic atrophy) is a very complex condition that can eventually lead to blindness.

“Once patients are diagnosed with dry AMD, it’s very hard to reliably predict how fast the disease will progress, and unfortunately there are currently no effective treatments available,” says Alan Stitt, Dean of Innovation and Impact and the McCauley Chair of Experimental Ophthalmology at Queen’s University Belfast. He also points to the challenge of diagnosing patients in an early stage of AMD when they still have vision left.

“In some respects, the early stages of dry AMD can be similar to other progressive back of the eye diseases like diabetic retinopathy. People may experience no appreciable changes to their vision until the disease has advanced to the stage where damage has already occurred. Often only at this stage do they consult a doctor or ophthalmologist, when it can already be too late. Moreover, dry AMD condition is complex with variation in how the disease manifests and progresses from patient to patient.”

The wet form of AMD is distinct from dry AMD and results from an abnormal growth of blood vessels in the retina. The vessels start to leak, causing fluid accumulation and possible scar formation. Vision loss can be very rapid, affecting 10-15% of patients with wet AMD. “Fortunately, for this type of the disease there are therapies available. The most common and well-known is anti-VEGF therapy,” says Alan Stitt.

“With its solid R&D base, Oxurion could make a difference.”

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Dry AMD, also called geographic atrophy, affects 85-90 % of people with late AMD. It involves degeneration of several cell types inside the retina, like photoreceptors, the retinal pigment epithelium (RPE), and the blood vessel network in the choroid underneath the RPE. Research companies across the globe are working hard to find an innovative cure by focusing on one or more of these cell types and prevent their damage during AMD.

Complex interaction

“Dry AMD arises from dysfunctional interactions between all these retinal and choroidal cells. This disruption of normal retinal function can lead to overt pathology and vision loss. The process is often slow with abnormalities being indicated by accumulation of small deposits, called ‘drusen’, underneath the retina. These drusen act as important sentinels of disease progression and indicate age-related pathology. Drusen accumulation alongside changes such as loss of pigment in the RPE, changes to choroidal blood flow and depletion of photoreceptor cells indicate worsening disease although this can occur over many years. Of course, there is variation between patients, and we don’t really know how rapidly some of them will progress,” says Alan Stitt.

He stresses that the disease is quite devastating and severely affects the life quality of older people. “They may eventually lose their central vision, which is essential for reading, driving, recognizing other persons… It can make the difference between living independently or not.”

Dry AMD has been under research for years but there is still no effective therapy or cure. Like other age-related diseases, adopting a healthy life-style with a balanced diet and definitely no tobacco use reduces the risk of developing AMD. “Dietary supplements might be protective, but this should definitely not be seen as a treatment for patients who have already developed the disease.”
Challenges and opportunities in research

“Huge opportunities lie in the treatment of AMD. Part of the challenge for scientists is to fully understand the nuances of what causes the onset and progression of the disease. We can partly meet this challenge by developing improved preclinical models. These models can be an important tool to identify therapeutic targets which can be matched to the right group of patients with dry AMD. Ideally this would occur very early in the disease process when there is still serviceable vision. It would already be a huge step for ophthalmic science and healthcare if we could halt this disease in its early early-stages by using an effective drug intervention,” he says.

Alan Stitt lauds Oxurion’s solid R&D in retinal diseases like diabetic retinopathy and related pathologies such as leakage, inflammation, and neurovascular degeneration.

“This knowledge base offers a strong foundation to start examining other back of the eye diseases like AMD. There could be interesting overlaps between some of the hallmarks of diabetic eye disease and age-related macular degeneration. Oxurion’s core expertise in retinal disease places them in a unique and promising position for the near future.”

About Alan Stitt

Prof. Alan Stitt was appointed to the McCauley Chair of Experimental Ophthalmology at Queen’s University Belfast in March 2001. For over 10 years he was Director of the Centre for Vision & Vascular Science (CVVS), then the reconfigured Centre for Experimental Medicine. He is now Dean of Innovation and Impact in the Faculty of Medicine, Health and Life Sciences.

He is internationally known for his research in ophthalmology. His academic strengths are reflected in his publication output, which has garnered numerous citations. He has been awarded leading prizes including election to the Royal Irish Academy (RIA), and award of a Royal Society Merit Award, and the Sir Jules Thorn Biomedical Science Award. He is a leading contributor to the academic community by assuming editorial responsibility, holding editorial board memberships for various journals, serving on advisory panels, and presenting guest lectures across the world.

Prof. Stitt’s research has focused on the pathogenesis of diabetic retinopathy and age-related retinal disease, where he discovered the role of advanced glycation end products (AGEs) and their receptors in the progression of these diseases. His work has uncovered several inter-related pathways involved in neuroglial and microvascular dysfunction in the diabetic and ageing retina. This research has led to developing and testing several compounds that have progressed to clinical trials.

(Source: Queen’s University Belfast)
Oxurion research update

Partnership to explore innovative molecules for dry age-related macular degeneration

With clinical development progressing well, Oxurion continues to invest in new pathways to treat other back of the eye diseases for which treatments are lacking. It recently entered a strategic partnership to explore heparanase inhibitors for treatment of age-related macular degeneration (AMD) in early or intermediate stage and late stage geographic atrophy (also called dry AMD).

Age-related macular degeneration (AMD) is a leading cause of blindness with a high unmet need for treatment. In late AMD a subset of patients will develop abnormal growth of blood vessels drives, known as ‘neovascular’ or ‘wet’ AMD, for which the standard treatment is with anti-VEGFs.

But 85-90% of late AMD patients have geographic atrophy (GA), the so-called ‘dry’ form, in which retinal cells slowly degenerate and become dysfunctional. There is currently no therapy to treat dry AMD.

Oxurion, with its deep knowledge of the mechanisms of diseases affecting the back of the eye, is researching opportunities to develop novel therapies for conditions such as advanced dry AMD and wet AMD. The molecule THR-687, now in a clinical phase 1 trial to assess safety in patients with DME (diabetic macular edema), also has the potential to treat patients with wet AMD.

In November 2018 the company teamed up with Beta Therapeutics Pty Ltd (Canberra, Australia) to develop new heparanase inhibitors for treatment of dry AMD. Heparanase is an endoglycosidase that plays a key role in modifying the extracellular matrix and in inflammatory processes.

Oxurion will continue to develop candidates in-house and identify strategic licensing opportunities and partnerships for new eye disease indications with high unmet needs.

What is AMD?

Age-related macular degeneration (AMD) is a leading cause of blindness. A study found that some 196 million people globally will likely be affected by AMD by 2020.*

It is known that abnormal angiogenesis drives one sub-type of AMD, known as ‘wet’ AMD. But most late AMD patients have geographic atrophy (GA), the so-called ‘dry’ form, in which retinal cells slowly degenerate and become dysfunctional. There is currently no therapy to treat dry AMD.

New treatment options for MacTel1

Macular telangiectasia type 1 (MacTel1) is a very rare condition typically affecting one eye. It usually occurs in men aged 40 to 50. It is a very degenerative disease that can lead to vision loss and for which there is currently no effective treatment. Oxurion is currently evaluating anti-PIGF (THR-317) in a clinical phase 2 study as a potential first-in-class therapy for MacTel1.
Clinical development update

Clinical phase 2 study started with THR-317 for treatment of MacTel1

This past year Oxurion took a major step in expanding its development pipeline to additional back of the eye disorders: it enrolled the first patient in a Phase 2 study evaluating THR-317 for treatment of MacTel1.

Macular telangiectasia is a degenerative vascular disease affecting the macula, the light-sensitive layer at the back of the eye that provides central vision and allows us to do everyday tasks like driving, reading, and recognizing faces.

There are two types of macular telangiectasia. Type 1, also called aneurysmal telangiectasia, is the less common form. It typically affects one eye and commonly occurs in men in their 40s or 50s. In MacTel1, capillaries of the macula become dilated and aneurysms form, causing swelling, disrupting blood flow, and often leading to leakage from the blood vessels.

Type 2, called perifoveal telangiectasia, is a bilateral neurodegenerative macular disease that is characterized by minimal dilatation of the parafoveal capillaries, hyperplasia of the retinal pigment epithelium, foveal atrophy, and subretinal neovascularization.

There is currently no cure or effective treatment for MacTel1. Physicians use laser therapy to help relieve the swelling of the blood vessels and reduce complications. Alternatively, intraocular steroids or intravitreal injections with anti-VEGF agents are used. Most patients with MacTel1, however, don’t respond well to anti-VEGFs, and laser or steroid treatment is considered quite intrusive.

Research suggests PlGF could play a key role in MacTel1, so Oxurion is assessing the potential of THR-317 (anti-PlGF) in this new disease area. The phase 2 clinical study plans to enroll 10 patients with macular edema caused by MacTel1, who will each receive 3 intravitreal injections with THR-317 over a two-month period. The therapy’s efficacy and safety will be assessed via functional and anatomic endpoints. The first results are expected by the end of 2019.
Clinical development pipeline
Solid research models and good intuition: the magic combination for successful clinical trials

Dr. Schlingemann has been a vitreoretinal specialist for many years as researcher, doctor, and professor at the University of Amsterdam. He is also founder of one of the leading ophthalmic clinical trial centers in the Netherlands. He is a leader in treating medical retinal disorders. Each year he supervises some 5,000 intravitreal injections and many clinical trial patients. Almost 1,000 patients are under active treatment.

The only way to cure retinal disorders is by joining forces

Dr. Schlingemann is passionate about medical R&D and enjoys his role as an Oxurion advisor. "Oxurion is developing a promising research pipeline and is active in exactly the same areas of expertise as I am. Being on their advisory board is a rewarding experience," he says.

Ophthalmologists and other medical professionals are usually well aware of new treatments once they’re established in the market, but they often don’t know what solutions are in the pipeline. As both an ophthalmologist and a researcher, Dr. Schlingemann moves between two worlds. He stresses the need for doctors, biotech companies and the pharmaceutical industry to work together. "The number of patients with retinal diseases will keep rising and we cannot cure all these people nor all these diseases by ourselves. It’s very valuable to collaborate in this developmental stage," he observes.

Two crucial factors for a successful pipeline

Dr. Schlingemann highlights two things that make the Oxurion pipeline unique and successful. "First of all, Oxurion has developed a very effective method for developing new drugs for back-of-the-eye diseases. This has always been a challenge in the field of retinal diseases, partly due to lack of functional research models. I think Oxurion works with the best models in the field, plus they have them in-house." The second key success factor. "Good intuition and a competent research team with a good atmosphere. Oxurion relies on its own good judgment and doesn’t waste money on dead-end pathways whereas other research groups often keep digging. It stops research once it sees it’s not leading anywhere. The goal is to be a fast and agile biotech company characterized by quality and cross-functional teamwork. This collaborative mindset is Oxurion’s key strength."
A research pipeline aimed at lowering the treatment burden for patients

Oxurion’s pipeline conducts clinical trials with three molecules: THR-317, THR-149 and THR-687. Dr. Schlingemann sees great value in all three but suspects that THR-317 (also known as anti-PIGF) will prove the most impactful in clinical trials.

“Anti-PIGF is the one offering the most for patients by lowering the burden of treatment. Moreover, it can be used in combination with other therapies, such as anti-VEGF, where it could be effective in treating advanced-stage diabetic retinopathy.”

“Another exciting development for anti-PIGF is that phase 2 trials for treating MacTel1 have started. That’s hopeful news for patients who suffer from this very rare and hard-to-treat vascular disease.”
About Reinier Schlingemann

Dr. R.O. Schlingemann (1960) has been named Professor by Special Appointment of Ocular Angiogenesis in the Faculty of Medicine at the University of Amsterdam (AMC-UvA) since 2008, a chair designated on behalf of the Society for the Promotion of Physics, Medicine and Surgery. Since 2018 he is full Professor of Ophthalmology and Vascular Diseases of the Macula at the AMC-UvA, and also Invited Professor and Director of Research at the Jules-Gonin Eye Hospital, Fondation Asile des Aveugles and the University of Lausanne.

Conditions involving the growth (angiogenesis) and leakage of blood vessels in the eye are the major cause of untreatable blindness and impaired vision in the Western world. The focus of Reinier Schlingemann’s research is mainly on the role of growth factors in angiogenesis and wound healing in the eye, and on vascular leakage as a cause of macular edema. In addition, he conducts research into the mechanisms that cause diabetic retinopathy and age-related macular degeneration. With his research, Schlingemann has played an important role in the introduction of new medicines that inhibit angiogenesis. In addition to this more fundamental research, he has also set up a clinical trial centre within his department for ophthalmic clinical studies. Schlingemann has also played an important role in establishing a network of similar centres in the Netherlands. Under his leadership, from 2008 onwards this network started three major nationwide comparative studies into the angiogenesis inhibitors Avastin and Lucentis in treating age-related macular degeneration and macular edema in diabetes and retinal vein occlusions.

Since 1996, Schlingemann has worked as an ophthalmologist and as head of the Ocular Angiogenesis Group at the UvA Academic Medical Centre (AMC). Previously, he had worked as a researcher in London and Oklahoma City and at the University of Leden and Radboud University Nijmegen. Schlingemann was also affiliated with the Moorfields Eye Hospital in London as fellow ophthalmologist and senior honorary registrar in the medical retina service of Professor Alan Bird. Schlingemann is a member of the board of the National Foundation for the Blind and Visually Impaired and the Medical Retina Working Group of the Netherlands Ophthalmic Society. He was also a member of the editorial committees of the Netherlands Tijdschrift voor Geneeskunde (Netherlands Journal of Medicine), Ophthalmic Research and the Nederlands Tijdschrift voor Diabetologie (Netherlands Journal of Diabetology). For his research into eye conditions caused by diabetes, Schlingemann has received various project grants and the 2010 Research Award from the Netherlands Diabetes Fund.
THR-317, an anti-placental growth factor (anti-PIGF) with a mechanism to act against hyperpermeability, is being developed to increase the efficacy of standard of care therapy and decrease the treatment burden for patients with DR and DME. By reducing leakage of blood vessels, it can halt early-stage inflammation in NPDR and prevent further progression of edema, angiogenesis and fibrosis. Since anti-PIGF also tackles fibrosis and inflammation, it also has the potential to treat PDR patients if used in combination with anti-VEGF therapy with alternating injections.

Oxurion has initiated a Phase 2 clinical study and has recently completed the recruitment of 70 patients to investigate the efficacy and safety profile of THR-317 in combination with anti-VEGF (Lucentis®) for the treatment of diabetic macular edema (DME).

Oxurion is also evaluating THR-317 as a potential first-in-class treatment for idiopathic macular telangiectasia type 1 (MacTel 1) in a Phase 2 clinical trial.
THR-149 (PKal Inhibitor)

THR-149 is a plasma kallikrein (PKal) inhibitor for treatment of DME. Through the inhibition of the plasma kallikrein-kinin (PKal-kinin) system, THR-149 prevents the induction of retinal vascular permeability, inflammation and angiogenesis. Literature data show that patients with DME have elevated levels of plasma kallikrein and that the vitreous level of plasma kallikrein varies less compared to VEGF, making it a potentially more effective target for the treatment of DME. Oxurion has enrolled the first patient in a phase 1 clinical study evaluating THR-149 for treatment of DME.

Oxurion is actively recruiting patients for a Phase 1 clinical study that is currently underway to evaluate THR-149 for the treatment of DME.

THR-687 (Pan RGD integrin antagonist)

THR-687, a pan RGD integrin antagonist, targets a broader spectrum of DR hallmarks. Preclinical models show that it is a potent inhibitor of angiogenesis-induced vascular leakage. The inhibition of integrins targets multiple processes involved in pathological angiogenesis and vascular leakage, unlike anti-VEGF treatment.

Oxurion is actively recruiting patients for a Phase 1 clinical trial to assess the safety of THR-687 in patients with DME.
Pipeline overview

Pipeline legend

- **THR-317**
  Diabetic Retinopathy, DME, MacTel1

- **THR-149**
  DME

- **THR-687**
  Diabetic Retinopathy, DME

- **Research in dry AMD**
Jetrea: unlocking opportunities

JETREA® (ocriplasmin) is the first and only pharmacological treatment for symptomatic vitreomacular adhesion and vitreomacular traction (sVMA/VMT). Oxurion owns the global commercial rights to this product and will capitalize on the opportunities and potential to commercialize Jetrea further on a global scale to the benefit of patients.
Oxurion commercial update

Jetrea: solid foundations for further growth

Regaining the global commercial rights to Jetrea was definitely a milestone in Oxurion’s history. The company set up a dedicated global commercial team. This past year it took over all global commercial activities, and successfully secured access and transferred marketing authorization for Jetrea.

“Transferring a drug’s marketing authorization from one company to another involves many regulatory aspects, country-specific requirements, and pharmacovigilance issues,” explains Vinciane Vangeersdaele, Chief Commercial Officer. “The challenge was to maintain pricing and reimbursement levels in all key markets. The team worked hard with reimbursement agencies around the world to secure access. All reimbursement conditions are maintained.”

**Transfer of all commercial activities**

Oxurion also set up a centralized distribution center in Belgium, where Jetrea is labeled and packed and the customer service department is located. From this center the product is shipped to all countries. Oxurion was able to take over all shipments and commercial activities in September 2018, less than a year after transfer of the global rights.

“That was quite a milestone for the team: transferring the ordering and billing process and the whole supply chain, and informing all customers and users. At the same time we brought the new, already-diluted formulation of Jetrea onto the European market. We leveraged our experience in the US market and the new formulation was accepted very well by all customers.”

**Interaction with customers**

The team is now determined to develop a growth strategy for Jetrea. “Our main focus is to communicate and interact with the larger eye community, face-to-face if possible. This past year, for example, we’ve had a commercial booth at several international congresses. These events allow us to talk to our customers, understand their needs, find where our product can bring the most value, and convince physicians of the benefits of using Jetrea.”

More than 30,000 patients across the globe have now been treated with Jetrea, yielding more real-life, evidence-based information. “We now have a very good idea of which patients benefit the most from it. That is why, in
our commercial strategy, we apply a targeted approach to a certain subset of patients for whom Jetrea really brings added value,” adds Vinciane Vangeersdaele.

Further empirical evidence, from studies like ORBIT in the US and OVID in Europe and Canada, supports that strategy. Recent findings from these are consistent with the last randomized control trial. The data also reveal excellent benefits in patient outcomes when the appropriate patient profile is selected.

**Key markets**

Oxurion now has marketing teams in three key markets: the US, Germany, Italy. “We are also preparing for the UK to set up a dedicated marketing team there. That allows us to have close contact with local customers.” The company also closely assessed and analyzed the market, producing a more targeted approach for the future with a focus on certain countries. For the near future Oxurion is looking at Canada, Switzerland, Austria, Spain, Portugal, Greece, France and home-market Belgium.

“It was a very conscious decision to concentrate on the markets with growth opportunities,” explains Vinciane Vangeersdaele. “Everything we do pursues the goal of bringing value to patients and fulfilling our ambition to grow. We’re on the right track to deliver on these promises.”
“HIGH SUCCESS RATE WHEN USING THE RIGHT SELECTION CRITERIA”

As a vitreo-retinal specialist, Dr. Arshad Khanani treats about 12,000 patients a year with vision problems. About 100 of them are diagnosed with sVMA/VMT. “That number is still increasing every year. It is good to have an alternative option for patients in addition to vitrectomy,” he says.

Dr. Khanani started using Jetrea when it came on the market in 2013. “Initially it wasn’t easy to reach a high success rate. It became clear it was really a matter of selecting the right patients who can benefit most from it. I managed to find the right selection criteria and am using the product on many patients: my success rate is now 50-75% with Jetrea.”

Dr. Khanani values Jetrea for providing an added option for treating sVMA/VMT. “Now we have four ways to manage the disease: observe patients when they have no symptoms yet, treat them with acrplasmin when we see certain characteristics, consider pneumatic vitreolysis (but I don’t use it as there are no prospective trials done with that technique), or vitrectomy. Ocriplasmin especially works well when the patient has sVMA/VMT with a small macular hole, less than 250 microns, or just vitreomacular traction without other problems like broad adhesion or epiretinal membrane (ERM).”

“We have learned a great deal in the past five years about how the product works. There is much literature now, including data from the ORBIT study and publications from retina specialists who use Jetrea. We can use all these data and criteria to guide physicians to a high success rate in all their patients.”

“WELL UNDERSTOOD AND PROVEN TREATMENT”

Dr. David Steel sees 70-80 patients with symptomatic VMT per year. “Carefully assessing the symptoms and clinical signs are a critical aspect of treating patients with the appropriate therapy, whether that be observation, treatment with Jetrea, or a vitrectomy,” he says.

Five years after Jetrea’s launch, Dr. Steel calls it a licensed and proven option to treat people with symptomatic VMT. “There is substantial literature now about how acrplasmin works, its pros and cons and the risks and benefits of the treatment.”

“For instance, we know now that patients with small macular holes are twice as more likely to have a successful outcome with Jetrea, as compared to medium sized ones. I can think of a number of patients with early macular holes who were treated and were very pleased with the outcome. They get excellent results in their vision, so acrplasmin can be a fantastic therapy. On the other hand, we also know that when people have additional conditions like dry AMD or DME the outcome can be less successful.”

He confirms that selecting the right people for a treatment with Jetrea makes all the difference. “The success rate can be up to 60-70% but you really need to study your patients. There are a number of positive predictor factors that physicians can take into consideration including phakia and the absence of associated epiretinal membrane.”

“It is also very important to inform patients of the risks and benefits of all possible treatments. A vitrectomy is very effective but also more intrusive and entails a risk. An injection with acrplasmin is less intrusive, but still carries some risk. Patients need to know there are often side effects particularly in the first 24 to 48 hours but their vision will typically improve again after the first 2 or 3 weeks.”
Oncurious: developing alternative treatments for cancer

As an R&D company Oxurion excels in researching the retinal space and diabetic eye diseases. Its daughter company Oncurious (a joint venture with VIB) pursues the same groundbreaking work in a different field: oncology.
**What is medulloblastoma?**

Medulloblastoma is a tumor in the brain. It is very rare in adults but the most common type of malignant brain cancer in children. The tumor grows invasively at the base of the skull and spreads rapidly through the cerebrospinal fluid to other parts of the body.

**Symptoms**
- behavioral changes
- appetite changes
- headache, nausea, vomiting, drowsiness
- unusual eye movements

**What are treatment options?**
The most common treatments for children are:
- surgical removal of the tumor
- radiation and/or chemotherapy

These raise the chance of survival but are very damaging to a child’s developing brain and are associated with significant morbidity and neurocognitive impairment. The prognosis is worse for children younger than 3, when not all of the tumor can be removed, or when the cancer has spread to other parts of the body.

**TB-403 (anti-PIGF)**

Oncurious is developing the first targeted alternative therapy to treat this rare life-threatening tumor. Medulloblastoma causes an unfavorable increase in production of PIGF cells. Anti-PIGF can block the PIGF signals, which creates a significant impact. The first clinical studies suggest this anti-PIGF treatment leads to tumor regression, decreased metastasis and higher survival rates.

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**Perspectives**

**TB-403 as an alternative therapy for medulloblastoma**

Oncurious’ research team is working to develop an alternative treatment for pediatric brain tumors. It is investigating whether TB-403 (an anti-PIGF) can treat aggressive medulloblastoma in young patients. The latest findings are very promising. A US Phase 1/2a study is ongoing and aims to recruit 27 patients with Relapsed or Refractory Medulloblastoma. For recruiting patients, Oncurious is partnering with Beat Childhood Cancer, an international group of researchers and hospitals dedicated to finding a way to stop childhood cancers. The study is currently enrolling the 4th and last cohort of patients. Initial data from this study are anticipated towards the end of 2019.

**Cancer immunotherapy**

The first generation of immunotherapies for treating cancer has just entered the market. Oncurious, already thinking of the future, now wants to take immuno-oncology research to the next level.

Two years ago, Oncurious joined forces with VIB (Flanders Institute for Biotechnology) and acquired a portfolio with five innovative immuno-oncological assets. Clinical trials with these five molecules could lead to a breakthrough in oncological treatments. Immunotherapy is an alternative and/or complementary treatment to chemotherapy, radiation, and surgical removal of tumors. Its basic idea is to use the body’s own cells to fight cancer cells. Many patients still don’t respond well to first-generation immunotherapies, so this research is very valuable.
About us

Oxurion at a glance

Oxurion is a biopharmaceutical company developing treatments to preserve vision for patients with diseases affecting the back of the eye. It has engineered a diverse portfolio of disease-modifying drug candidates, including treatments for diabetic eye disease, a leading cause of blindness in people of working age worldwide.

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

Oxurion is headquartered in Leuven, Belgium, and is listed on Euronext Brussels under the symbol OXUR.

Oxurion is headquartered in Leuven, Belgium, and is listed on the NYSE Euronext Brussels exchange under the symbol OXUR.
Our team

People at Oxurion

Oxurion employs 78 people worldwide, all are united by a shared goal: to make Oxurion a global leader in developing and commercializing innovative treatments for chronic eye disorders.

Most members of the Oxurion international team hold a master’s or PhD degree. The majority work at our headquarters in Leuven (Belgium) or from our office in New Jersey (U.S.).

Each member of the Oxurion team provides a distinct viewpoint and set of experiences in the biopharmaceutical industry. The diversity and experience of the team stimulates creativity and problem-solving while enabling the company to successfully develop and commercialize therapeutics to preserve the vision of patients worldwide.
Management Team
Our management team’s expertise and experience in research, clinical development, commercialization and financing is what ensures Oxurion’s long-term success. The Executive Committee sets the company’s vision and strategy, which the management team then plans and executes. CEO and MD Patrik De Haes and CFO Dominique Vanfleteren oversee the company’s daily management.

Patrik De Haes, MD, Chief Executive Officer
Patrik De Haes, MD, has over 25 years of experience in the global healthcare industry in product development, marketing and general management. Before joining Oxurion as CEO in 2008, Patrik was head of Roche’s Global Insulin Infusion division. Prior to that he was President and CEO of Disetronic Medical Systems Inc., a medical device company based in Minneapolis, USA. He also led the global development and commercialization of the first biotech product at Sandoz Pharma (now Novartis) in Switzerland. Patrik holds a degree in Medicine from the University of Leuven.

Dominique Vanfleteren, Chief Financial Officer
Dominique Vanfleteren has over 25 years of experience in senior finance, operational, control and reporting roles in quoted international biopharmaceutical companies. Before joining Oxurion, Dominique spent 12 years at UCB, a global biopharmaceutical company, where he held a number of international managerial finance positions, the latest in Brussels and Shanghai as CFO of UCB’s Asia Pacific Operations. Prior to UCB, he worked for GSK for 16 years in senior finance positions in Brussels and London, the latest as Finance Director of GSK’s Diversified Healthcare Services Europe. Dominique holds a bachelor’s degree in Civil Engineering and a master’s in Applied Economics (UCL).
Board of Directors
The company is led by a collegiate Board of Directors which is the company’s most senior administrative body. The Board of Directors decides upon the company’s values and strategy, upon its willingness to take risks and upon the general policy plan. The Board of Directors currently consists of six members.

Thomas Clay
Chairman, Non-Executive, Independent Director

Patrik De Haes, MD
ViBio bvba, Executive Director

Adrienne Graves, PhD
Non-Executive, Independent Director

David Guyer, MD
Non-Executive Director

Emmanuèle Attout
Investea SPRL, Non-Executive, Independent Director

Baron Philippe Vlerick
Non-Executive, Independent Director
Shareholders information

Listing
Oxurion is listed on Euronext Brussels under the symbol OXUR.

Investor relations
Our investor relations policy includes:

- Providing reliable, accurate and valuable information in a timely manner to help shareholders make informed decisions.
- Full transparency
- Operating within the company’s policies and adhering to relevant security laws and regulations
- Strengthening our dialogue with the investment community
- Providing access to the senior management team

Shareholding structure
As of 31 December 2018, Oxurion has a total number of 38,291,950 outstanding shares and a total number of 1,174,750 warrants.

<table>
<thead>
<tr>
<th>Shareholder</th>
<th>% of voting rights</th>
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<tbody>
<tr>
<td>Mr Thomas M. Clay and entities controlled by him</td>
<td>4.68%</td>
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<tr>
<td>Mrs Lavinia D. Clay</td>
<td>4.10%</td>
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<tr>
<td>Baron Philippe Vlerick and entities controlled by him</td>
<td>6.07%</td>
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<tr>
<td>Novartis Pharma AG</td>
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<td>Public</td>
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Paying agent services
KBC Bank acts as the paying agent. The paying agent will not charge shareholders with respect to payments of dividends, the exercise of subscription rights and other events concerning Oxurion shares. Shareholders should inform themselves about the amounts that other financial intermediaries may charge in connection with paying agency services.

Financial calendar

<table>
<thead>
<tr>
<th>Date</th>
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</thead>
<tbody>
<tr>
<td>07 May 2019</td>
<td>Annual Shareholder’s Meeting</td>
</tr>
<tr>
<td>08 May 2019</td>
<td>Business Update Q1 2019</td>
</tr>
<tr>
<td>05 Sep 2019</td>
<td>Half Year Results FY 2019</td>
</tr>
<tr>
<td>18 Oct 2019</td>
<td>Business Update Q3 FY2019</td>
</tr>
</tbody>
</table>
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