

Oxurion NV Business Update - Q1 2020

Progressing Clinical Development of Next Generation Therapies for Diabetic Eye Disease – Beyond anti-VEGF

Total Cash & Investments at €43.8 million as of March 31, 2020

Highlights

- Positive data from Phase 1 study evaluating THR-687 (Pan-RGD integrin antagonist) for the treatment of Diabetic Macular Edema (DME) announced in January 2020.

Preparations for planned Phase 2 study with THR-687 in DME on-going. Study expected to start in H1 2021.
- Phase 2 study with THR-149 in DME is now expected to start H2 2020, or as soon as COVID-19 related safety considerations allow. Preparations progressing as planned.
- At the end of March 2020, Oxurion had cash, cash equivalents & investments of €43.8 million.

Leuven, Belgium, May 7, 2020 – 17.45 PM CET – [Oxurion NV](#) (Euronext Brussels: OXUR), a biopharmaceutical company engaged in the development of next generation therapies to treat diabetic eye disease, today issues its business and financial update for the three-months ending March 31, 2020.

Oxurion continues to progress the development of its pipeline of innovative drug candidates for treating Diabetic Macular Edema (DME). Diabetic eye disease, including DME, is a significant global healthcare problem and the major cause of blindness in adults of working-age.

Oxurion's clinical development pipeline consists of novel products with different, including non-VEGF, modes of action, which potentially give the Company access to a significant share of the large and fast-growing diabetic eye disease market.

Oxurion's clinical pipeline comprises of

- **THR-149:** a potent plasma kallikrein inhibitor completed a Phase 1 multicenter, dose escalation study for the treatment of DME in July 2019. Positive data showed that THR-149 is well-tolerated and safe with no dose-limiting toxicities or drug-related serious adverse events reported. The data also showed promising efficacy results in relation to Best Corrected Visual Acuity (BCVA) after a single injection and for up to 90 days of follow up.
- **THR-687:** a small molecule pan-RGD integrin antagonist is being developed to treat a broad range of patients with diabetic eye disease. A Phase 1 study was completed in January 2020 and the data showed it to be well-tolerated and safe. The data also showed promising efficacy results with rapid onset of action and prolonged improvement in BCVA following a single injection.

Patrik De Haes, M.D., CEO of Oxurion, commented:

“The positive Phase 1 results that we announced in January from the Phase 1 trial with THR-687 have strengthened Oxurion’s position as a leader in developing safe and effective next generation therapies for DME and diabetic eye disease.

Based on the preclinical and clinical data to-date, THR-687, a small molecule pan-RGD integrin antagonist, clearly has the potential to deliver improved clinical benefits to a broader population of patients with diabetic eye disease than currently approved anti-VEGF treatments.

We are preparing a Phase 2 study with THR-687 which is expected to start in H1 2021.

We have delayed the start of our planned Phase 2 study evaluating multiple doses of THR-149 in patients with DME due to the current Covid-19 pandemic. We are continuing to prepare for this important trial and expect the study to start as soon as conditions allow us to proceed in an efficient manner, taking into account the safety of everyone who will be involved.

Our current cash position of €43.8 million will allow us to develop these exciting next generation therapies designed to provide both patients and physicians with improved treatment options for diabetic eye disease through mid-2021.”

Diabetic Eye Disease – Oxurion’s key focus

Diabetic eye disease is caused by the high blood glucose levels (hyperglycemia) associated with diabetes. If left unchecked, hyperglycemia causes damage to the capillaries supplying blood, and hence oxygen, to the retina, the structure at the back of the eye responsible for vision.

Diabetic eye disease includes Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME).

DR is the presence and characteristic evolution of typical retinal microvascular lesions in an individual with diabetes, leading to damage to the blood vessels in the retina. DR is a chronic, progressive, sight-threatening, and life-altering disease, and is the leading cause of vision loss in working-age adults (20-65 years).

DR can be further classified by severity types, non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

DME, which is a consequence of DR, can occur at any stage in the development of DR. DME is an accumulation of fluid in the macula (central part of the retina) due to leaking blood vessels, leading to swelling of the macular area due to the increased permeability of the vessels.

More than one in three people living with diabetes will develop some form of DR in their lifetime. Almost one in three people living with DR have some vision-threatening form of the disease such as DME and/or PDR.

DR and DME are a growing public health concern due to the rapid growth in the number of people with diabetes globally.

An estimated 37.8 million people have been diagnosed with diabetes in the United States (US), European top five countries (EU5) (France, Germany, Italy, Spain, and the United Kingdom), and Japan. If the undiagnosed population is included, the total number of persons with diabetes in these countries is estimated to increase to 61.3 million people.

The prevalence of DME was estimated to be 2.8 million people in the US, EU5 and Japan in 2019. The market value for DME treatments in these markets was estimated to be worth between approximately \$3.4 to \$3.8 billion in 2019.

The market for DME therapies is dominated by anti-VEGFs, which are the current standard of care. However, anti VEGFs have been shown to deliver sub-optimal results in a significant portion of the patient population. Around 40% of DME patients have an unsatisfactory early visual response with anti-VEGF therapy, and in many cases anti-VEGFs fail to achieve a clinically meaningful visual improvement.

Oxurion is focused on solving these unmet medical needs in diabetic eye disease.

Next generation therapies for improved outcomes in DME – Beyond anti VEGF

Oxurion has developed a state-of-the-art ophthalmology research and development model geared at identifying and developing treatment methodologies for complex retinal diseases with large unmet needs.

Oxurion's R&D activities are focused on using its in-depth understanding of important eye disease mechanisms to generate new therapies that can be game changing in the treatment of several major retinal indications such as diabetic eye disease, including DME.

In general, treatment of diabetic eye disease is centered around anti-VEGF therapies, which are used to treat approximately 80% of patients. Despite the significant success of anti-VEGFs, there will always be a need from both physicians and patients for improved therapies that have:

- Faster onset of action
- Better therapeutic effect in terms of visual function, BCVA, and response rate (proportion of patients)
- Longer duration of response allowing extended treatment intervals
- Improved convenience of treatment through a simpler dosing regimen

Those requirements are driving the development of Oxurion's new generation of therapies, beyond anti-VEGF.

Applying these criteria, Oxurion is developing THR-687 and THR-149 to meet specific unmet needs in the market for diabetic eye disease therapies.

Both candidates are being prepared to start Phase 2 clinical trials.

Positive Phase 1 Results with THR-687 for the treatment of DME – Phase 2 program expected to start in H1 2021

Oxurion is developing THR-687, a novel pan-RGD integrin antagonist, to preserve vision in a broad range of patients with diabetic eye disease. This wide-ranging potential is based on the hypothesis that integrin inhibition can address many of the processes that result in the pathological angiogenesis and vascular leakage that cause diabetic eye disease and other retinal diseases.

Topline data from the Phase 1 trial showed that THR-687:

- Is well-tolerated and safe with no dose-limiting toxicities. No serious adverse events were reported at any of the doses evaluated in the study.
- The study also looked at efficacy including changes to the patient's BCVA. Across all doses, a rapid onset of action as measured by mean BCVA change was observed from Day 1 with an increase of 3.1 letters, which further improved to 9.2 letters at Month 1.
- This activity was maintained with a mean BCVA improvement of 8.3 letters at Month 3 following a single injection of THR-687.
- A clear dose response was seen in terms of BCVA with the highest dose of THR-687 delivering a mean BCVA Improvement of 11 letters at Day 14, with a peak improvement of 12.5 letters at Month 3.
- In addition, a peak mean central subfield thickness (CST) decrease of 106 µm was observed at Day 14 with the highest dose of THR-687.

Data from this positive Phase 1 study with THR-687 were presented by a leading retina expert at the Bascom Palmer Eye Institute Angiogenesis, Exudation, and Degeneration 2020 Meeting in February 2020 in Miami (US).

Oxurion is preparing a Phase 2 study with THR-687 which is expected to start in H1 2021.

THR-149 – a plasma kallikrein inhibitor for treatment of DME

Positive Phase 1 Results with THR-149 for the treatment of DME – Phase 2 program expected to start as soon as COVID-19 related safety considerations allow an efficient study

THR-149 is a novel plasma kallikrein inhibitor being developed as a potential new standard of care for the 40% of DME patients who respond sub-optimally to anti-VEGF therapy.

THR-149 acts through inhibition of the Plasma Kallikrein-Kinin (PKaI-Kinin) system, a validated target for DME.

The Phase 1 study for THR-149 showed that it:

- Is well-tolerated and safe. No dose-limiting toxicities nor drug-related serious adverse events were reported at any of the dosages evaluated in the study.
- Delivered promising results in relation to efficacy, particularly improvements in the patient's BCVA. A rapid onset of action was observed from Day 1, with an increasing average improvement in BCVA of up to 7.5 letters at Day 14.

Importantly, this activity was maintained with an average improvement in BCVA of 6.5 letters at Day 90 following a single injection of THR-149.

Data from this positive Phase 1 study with THR-149 were presented at several major retina conferences in Europe and the US in 2019, including the European Society of Retina Specialists (EURETINA) in Paris and the Retina Society Annual Meeting in London.

The Company is currently preparing to start a Phase 2 development program, which will evaluate multiple doses of THR-149 in patients with DME. This study is expected to start as soon as COVID-19 related safety considerations allow an efficient study to be undertaken.

This novel drug candidate was generated using Bicycle Therapeutics' Bicycles[®] technology platform.

Global commercial license agreement for JETREA[®] signed allowing resources to be focused on our next generation diabetic eye disease pipeline

In March, Oxurion announced the signing of a JETREA[®] global commercial license agreement with **Inceptua Group**.

Inceptua Group is a global pharmaceutical company and service partner spanning the product lifecycle – from clinical trials, through early access programs to licensing and commercialization of products. The Group has offices in Europe, the US and Asia.

Financial Update

The Oxurion cash position (incl cash equivalents & investments) at end of March 2020 was € 43.8 million. This compares with €52.9 million at the end of December 2019.

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About Oxurion

Oxurion (Euronext Brussels: OXUR) is a biopharmaceutical company developing next generation standard ophthalmic therapies, which are designed to better preserve vision in patients with diabetic eye disease, the leading cause of blindness in people of working age worldwide.

Oxurion's clinical pipeline comprises:

- THR-149, a plasma kallikrein inhibitor being developed as a potential new standard of care for DME patients who respond sub-optimally to anti-VEGF therapy.

THR-149 has shown positive topline Phase 1 results for the treatment of DME. The Company is currently preparing to conduct a Phase 2 clinical program, which is now expected to start as soon as COVID-19 related safety considerations allow an efficient study. THR-149 was developed in conjunction with Bicycle Therapeutics PLC (NASDAQ: BCYC)

- THR-687, is a pan-RGD integrin inhibitor, that is initially being developed as a potential new standard of care for all DME patients

Positive topline results in a Phase 1 clinical study assessing it as a treatment for DME were announced in January 2020. THR-687 is expected to enter a Phase 2 clinical trial in H1 2021. THR-687 is an optimized compound derived from a broader library of integrin inhibitors in-licensed from Galapagos NV (Euronext & NASDAQ: GLPG).

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

More information is available at www.oxurion.com

Important information about forward-looking statements

Certain statements in this press release may be considered “forward-looking”. Such forward-looking statements are based on current expectations, and, accordingly, entail and are influenced by various risks and uncertainties. The Company therefore cannot provide any assurance that such forward-looking statements will materialize and does not assume an obligation to update or revise any forward-looking statement, whether as a result of new information, future events or any other reason. Additional information concerning risks and uncertainties affecting the business and other factors that could cause actual results to differ materially from any forward-looking statement is contained in the Company’s Annual Report. This press release does not constitute an offer or invitation for the sale or purchase of securities or assets of Oxurion in any jurisdiction. No securities of Oxurion may be offered or sold within the United States without registration under the U.S. Securities Act of 1933, as amended, or in compliance with an exemption therefrom, and in accordance with any applicable U.S. state securities laws.