

Oxurion NV Business Update – H1 2019

**Positive Topline Phase 1 Results with THR-149
(Plasma Kallikrein Inhibitor) for treatment of DME**

**Mixed Topline Results from exploratory THR-317 (anti-PIGF) Phase 2a
ranibizumab combination study for the treatment of DME**

**THR-687 (Pan-RGD Integrin Inhibitor)
Phase 1 study patient enrolment complete
Data read out by end of 2019**

Total Cash & Investments at €67.6 million as of June 30, 2019

Highlights

Pipeline

- Positive topline data reported from Phase 1 safety study evaluating THR-149 (Plasma Kallikrein Inhibitor) for treatment of DME
 - THR-149 is well-tolerated and safe with no dose-limiting toxicities or drug-related serious adverse events reported.
 - Rapid onset of action starting at Day 1 with increasing average improvement in Best Corrected Visual Acuity (BCVA) at Day 14 following a single injection of THR-149.
 - Activity maintained at Day 90 following a single injection of THR-149.
- Mixed topline data reported from exploratory Phase 2a combination study evaluating THR-317 in combination with ranibizumab for the treatment of DME
 - Combination therapy did not show increase in BCVA in the overall population at Month 3.
 - Certain improvement in mean BCVA at Month 3 observed with the combination therapy in poor (or non) responders to prior anti-VEGF, and with patients with poor vision - baseline BCVA ≤65 letters.
 - Topline data confirm THR-317 in combination with ranibizumab is safe and well-tolerated.
- Patient enrolment completed in Phase 1 safety study evaluating THR-687 (pan RGD integrin antagonist) for treatment of DME
 - Company anticipates data read out by the end of 2019.

Financial

- Oxurion reports €67.6 million in cash, cash equivalents & investments at the end of June 2019. This compares to €85.1 million at the end of December 2018.
- Oxurion reports €1.8 million Jetrea® revenues for the period ending June 30, 2019. The Company decided to impair the remaining Jetrea® intangible assets.

Leuven, Belgium, September 5, 2019 – 17.40 CET – [Oxurion NV](#) (Euronext Brussels: OXUR), a biopharmaceutical company developing innovative treatments to preserve vision in patients with diabetic eye disease, today issues its business and financial update for the six-month period ending June 30, 2019.

Oxurion is continuing to progress the development of its innovative pipeline of disease modifying drug candidates for diabetic eye disease, particularly DME.

The Oxurion clinical development pipeline consists of novel products with different modes of action, which, together 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:

- a potent plasma kallikrein inhibitor (**THR-149**) is in a Phase 1 multicenter, dose escalation study for the treatment of DME. Recent positive topline 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 very promising efficacy results in relation to BVCA.
- a human placental growth factor (PIGF) neutralizing monoclonal antibody (**THR-317**).
Topline results from an exploratory Phase 2a study evaluating the efficacy and safety of intravitreal THR-317 when administered in combination with ranibizumab (Lucentis®), for the treatment of DME. Oxurion is further analyzing all data and is evaluating its future plans for THR-317 in relation to the treatment of DME.

In addition, THR-317 is being evaluated in a Phase 2 study for the treatment of Idiopathic Macular Telangiectasia Type 1 (MacTel 1), a rare disease that affects the macula and can lead to vision loss. First data from this study are expected towards the end of 2019.

- a small molecule pan-RGD integrin antagonist (**THR-687**) being developed to treat a broad range of patients with diabetic eye disease. Phase 1 study with THR-687 completed patient enrolment in September 2019. Topline results from the Phase 1 study are expected by the end of 2019.

Patrik De Haes, M.D., CEO of Oxurion, said: *“The positive topline results from a Phase 1 study confirm that THR-149, a potent plasma kallikrein inhibitor is well-tolerated and safe for intra-ocular use, and provides a rapid and sustained gain in BCVA. We believe that these positive findings demonstrate that THR-149 holds the potential to become a best-in-class PKal inhibitor for the treatment of DME. We are looking forward to the upcoming ‘late breaking’ podium presentation at the upcoming Euretina Congress in Paris and are currently in full preparation of a follow- up Phase 2 clinical trial evaluating THR-149 starting in early 2020.*

“The recently reported topline results from an exploratory Phase 2 study evaluating THR-317 (anti-PIGF) in combination with ranibizumab for treatment of DME suggest that a combination therapy could play a certain role in the treatment of poor (or non) responders to prior anti-VEGF and with patients with a baseline BCVA of less or equal to 65 letters. We will continue to review and analyze these results, as well as last year’s reported positive Phase 1 results from the monotherapy study, before deciding on how to best position this program as we progress our overall clinical-stage portfolio of next-generation therapies for the treatment of DME. In making this decision, we will also take into account the outcome of the study evaluating THR-317 for treatment of MacTel1. The latter is expected for end of 2019.”

“Earlier this week we were happy to confirm that we have completed patient enrolment into our Phase 1 study evaluating the safety of our THR-687, a small molecule pan-RGD integrin antagonist for the treatment of DME. Topline data from this Phase 1 study will be reported before the end of 2019”, he continues.

“Our solid cash position of €67.6 million and prudent cash management will allow us to progress all of our ongoing and planned clinical and preclinical developments into 2021”, he concludes.

Diabetic Eye Disease - A Significant and Growing area of medical need

Diabetes is a major global healthcare problem with an estimated 425 million adults living with diabetes worldwide today. This number is expected to increase to over 625 million by 2045, according to the International Diabetes Federation.

Diabetic eye disease is caused by hyperglycemia (high blood glucose levels) 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 retinopathy (DR) is a serious, sight-threatening disease and the leading cause of vision loss among working-age adults. DR progresses from mild, non-proliferative to more severe or even proliferative stages (PDR). PDR, the more advanced stage of diabetic eye disease happens when the retina starts growing new fragile blood vessels, which often bleed into the vitreous leading to loss of vision.

It is estimated that there are 150 million diabetics with DR of which 50 million have vision threatening disease.

Diabetic macular edema (DME) is a severe complication of DR. DME is an accumulation of fluid in the macula – the part of the retina that controls detailed vision - due to leaking blood vessels. DME represents an area of major unmet medical need. The current standard of care, anti-VEGFs, have shown to deliver sub-optimal results. More than 50% of patients have an unsatisfactory early visual response with anti-VEGF therapy, and in many cases, they fail to achieve a clinically meaningful visual improvement.

Oxurion Clinical and Pre-clinical Development Update

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

Positive Topline Phase 1 Results with THR-149 for the treatment of DME – Phase 2 program expected to start in H1 2020

THR-149 is a novel plasma kallikrein inhibitor being developed for the treatment of DME.

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

Topline data from the trial showed that THR-149 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.

The study also showed very promising results in relation to efficacy, in particular changes to the patient's Best Corrected Visual Acuity (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.

Oxurion is currently preparing the complete data analysis from this Phase 1 study with THR-149. The Company plans to present further clinical data from the study at Euretina in Paris (8 September), at the Retina Society Meeting in London (12 September) and during the upcoming AAO meeting of October in San Francisco.

The Company intends to start a Phase 2 development program with THR-149 in H1 2020.

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

THR-317 – a Humanized mAb Against Human PlGF for the treatment of DME

THR-317 (anti-PlGF) is a recombinant humanized monoclonal antibody directed against the receptor-binding site of human placental growth factor (PlGF). THR-317 is being developed for the treatment of DME.

In 2018, positive Phase 1 data demonstrated the potential of THR-317 for treatment of diabetic macular edema in monotherapy. Topline results from that study showed strong safety data as well as first indications of clinical activity and durability of effect.

Following those positive results, the Company initiated a Phase 2a exploratory proof of concept study evaluating THR-317 in combination with ranibizumab (Lucentis®) for treatment of DME.

Mixed results from exploratory Phase 2a Clinical study evaluating THR-317 in combination with ranibizumab (Lucentis®) for treatment of DME

In August 2019, the Company announced the topline results from an exploratory 70 patient Phase 2a study evaluating the efficacy and safety of intravitreal THR-317 administered in combination with ranibizumab (Lucentis®) a VEGF inhibitor, for the treatment of DME.

The study showed that the combination did not produce an increase in BCVA in the overall population at Month 3.

Certain improvement in mean BCVA at Month 3 could be observed with the combination therapy in 2 pre-specified subgroups of interest:

- o poor (or non) responders to prior anti-VEGF, and
- o patients with poor vision - baseline BCVA ≤ 65 letters

Topline data confirmed that THR-317 in combination with ranibizumab is safe and well-tolerated.

Topline data from this exploratory Phase 2 combination study have been presented at the EURETINA conference in Paris on September 5, 2019.

Oxurion will further review and analyze the Phase 2 data before deciding on how to best position this program within its clinical-stage portfolio of next -generation therapies for the treatment of DME.

Phase 2 clinical study evaluating THR-317 for treatment of MacTel1

Oxurion is recruiting patients in a Phase 2 multi-center study evaluating the efficacy and safety of intravitreal THR-317 for the treatment of Macular Telangiectasia Type 1 (MacTel 1). MacTel 1 is a rare disease that affects the macula and can lead to vision loss. There is currently no effective treatment for MacTel 1.

This Phase 2 study plans to enroll a maximum of 10 patients with macular edema caused by MacTel 1. Each patient will each receive three 8mg intravitreal THR-317 injections over a period of 2 months. Efficacy and safety of the therapy will be assessed via functional and anatomic endpoints.

Initial results from this clinical study are anticipated by the end of 2019.

THR-687 – an integrin antagonist for treatment of DME

Phase 1 study evaluating THR-687, a novel pan-RGD integrin antagonist for the treatment of DME – recruitment completed

Oxurion is developing THR-687, a novel pan-RGD integrin antagonist, to preserve vision of 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.

Oxurion is initially targeting THR-687 for the treatment of DME.

In September, Oxurion completed recruitment of a Phase 1 multicenter, dose escalation study evaluating the safety of a single intravitreal injection of THR-687 for the treatment of patients with DME. Twelve patients were enrolled in the study.

Initial results from this study are anticipated by the end of 2019.

At the EURETINA conference in Paris pre-clinical data will be presented showing that THR-687 potently inhibits ocular fibrosis. The presentation will be given on 6 September 2019.

Ocriplasmin Update

First introduced in early 2013, Jetrea® is a first-in-class pharmacological vitreolysis therapy approved for treatment of symptomatic vitreomacular adhesion or vitreomacular traction.

Over 30,000 patients have been treated with Jetrea® to-date with real world clinical data confirming that the drug is a safe and effective early treatment for a well identified group of patients suffering from symptomatic vitreomacular adhesion or vitreomacular traction.

As a company, we continue to recognize the value of providing this clearly differentiated treatment option to those patients who can benefit from it.

Oxurion remains committed to work alongside its stakeholders to provide Jetrea® to patients in an operationally efficient and cost-effective manner.

Oncurious - next generation immuno-oncology therapies Update

Oncurious – €1.0 million grant from Flanders Innovation and Entrepreneurship (VLAIO)

Oncurious, is developing next-generation immuno-oncology drugs targeting a broad spectrum of cancers. Oncurious is a majority owned subsidiary of Oxurion. The remainder of the shares in the company are owned by VIB, a leading life sciences research institute, based in Flanders, Belgium.

In June 2019, Oncurious received a project grant of close to €1.0 million from Flanders Innovation and Entrepreneurship (VLAIO) to support the further pre-clinical development of its pipeline of next generation cancer immunotherapies.

The non-dilutive grant funding will be used to identify a number of multi-specific biologics with distinct modes of action against immunomodulatory targets. These candidates will then be assessed in pre-clinical tumor models, both as monotherapies and in combination with standard of care treatment.

TB-403 for medulloblastoma

Recruitment of patients with Relapsed or Refractory Medulloblastoma is on-going in a US Phase 1/2a study with Oncurious' lead program TB-403, a humanized monoclonal antibody against placental growth factor (PlGF).

The purpose of this study is to evaluate the safety and tolerability of TB-403 at the maximum tolerated dose in pediatric subjects with relapsed or refractory Medulloblastoma. TB-403 is being developed by Oncurious in conjunction with BioInvent International.

Financial Update

During the first six months of 2019, Oxurion booked €1.8 million Jetrea® revenues. This compared to €3.8 million for the same period in 2018. Based on these revenues, the company did proceed with the write-off of the remaining Jetrea® intangible assets.

For the first half of 2019, the group reported a gross profit of €0.6 million, compared to a gross profit of €2.6 million for the same period in 2018.

Oxurion's R&D expenses were €12.0 million during the first half year of 2019. In the same period of 2018, the R&D expenses were €13.3 million. The 2018 figure included a milestone payment of €1.0 million related to the development of THR-149.

Selling and marketing expenses amounted to €3.4 million compared to €2.5 million in the corresponding period of 2018. The increase is the result of the return of ex-US Jetrea® rights.

General and administrative expenses were €3.3 million. This compares to €2.9 million in the first half of 2018.

For the first half of 2019, Oxurion reported a net loss of €33.3 million (or €-0.87 per share) composed of a €16.9 million Jetrea® remaining intangible asset write-off and €16.4 million current losses. Net, the €16.4 million loss compares to €15.2 million for the same period in 2018.

As of June 30, 2019, Oxurion had €67.6 million in cash, cash equivalents and investments. This compares with €85.1 million as of the end of December 2018.

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About Oxurion

Oxurion (Euronext Brussels: OXUR) is a biopharmaceutical company currently developing a competitive pipeline of three disease-modifying clinical drug candidates for diabetic eye disease, a leading cause of blindness in people of working age worldwide. The pipeline comprises:

- THR-149, a plasma kallikrein inhibitor, that 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 expected to start in H1 2020
- THR-687, a pan-RGD integrin antagonist, which is in a Phase 1 clinical study assessing it as a treatment for diabetic retinopathy and DME. Topline results from this study are expected in late 2019
- THR-317, a PIGF inhibitor is being evaluated for treatment of diabetic macular edema (DME), as well as for the treatment of Idiopathic Macular Telangiectasia Type 1 (MacTel 1), a rare retinal disease that affects the macula and can lead to vision loss

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.

Consolidated key figures as at June 30, 2019

Unaudited consolidated statement of financial position

In '000 euro (as at)	30-Jun-19	31-Dec-18
Non-current assets	7,951	23,775
Current assets	72,210	91,089
Total assets	80,161	114,864
Total equity	72,284	105,310
Non-current liabilities	1,616	0
Current liabilities	6,261	9,554
Total equity and liabilities	80,161	114,864

Unaudited consolidated statement of profit and loss

In '000 euro (for the period ended on June 30)	2019	2018
Income	1,807	3,752
Operating result	-33,365	-15,664
Finance income	236	571
Finance expense	-175	-74
Result before income tax	-33,304	-15,167
Income tax expense	-7	-4
Loss for the period	-33,311	-15,171
Result per share		
Basic earnings/(loss) per share (euro)	-0.87	-0.39
Diluted earnings/(loss) per share (euro)	-0.87	-0.39

Unaudited consolidated statement of profit and loss

In '000 euro (for the period ended on June 30)	2019	2018
Income	1,807	3,752
Sales	1,804	3,750
Income from royalties	3	2
Cost of sales	-1,224	-1,117
Gross profit	583	2,635
Research and development expenses	-12,040	-13,349
General and administrative expenses	-3,329	-2,874
Selling expenses	-3,408	-2,541
Other operating income	1,720	465
Impairment losses	-16,891	0
Operating result	-33,365	-15,664
Finance income	236	571
Finance expense	-175	-74
Result before income tax	-33,304	-15,167
Taxes	-7	-4
Loss for the period	-33,311	-15,171
Attributable to:		
Equity holders of the company	-33,317	-15,028
Non-controlling interest	6	-143
Result per share		
Basic earnings/(loss) per share (euro)	-0.87	-0.39
Diluted earnings/(loss) per share (euro)	-0.87	-0.39

Unaudited consolidated statements of other comprehensive income

In '000 euro (for the period ended on June 30)	2019	2018
Loss for the period	-33,311	-15,171
Exchange differences on translation of foreign operations	29	-58
Other comprehensive income, net of income tax	29	-58
Other comprehensive income that will not be reclassified to profit or loss	29	-58
Total comprehensive income for the period	-33,282	-15,229
Attributable to:		
Equity holders of the company	-33,288	-15,086
Non-controlling interest	6	-143

Unaudited consolidated statement of financial position

In '000 euro	30-Jun-19	31-Dec-18
ASSETS		
Property, plant and equipment	489	614
Right-of-use assets	2,453	0
Intangible assets	1,982	20,450
Other non-current assets	127	127
Non-current tax credit	2,900	2,584
Non-current assets	7,951	23,775
Inventories	413	1,036
Trade and other receivables	3,723	4,219
Current tax receivables	474	707
Investments	20,475	20,475
Cash and cash equivalents	47,125	64,652
Current assets	72,210	91,089
Total assets	80,161	114,864
EQUITY AND LIABILITIES		
Share capital	137,564	137,564
Share premium	13	13
Cumulative translation differences	-244	-273
Other reserves	-12,307	-12,563
Retained earnings	-53,170	-19,853
Equity attributable to equity holders of the company	71,856	104,888
Non-controlling interest	428	422
Total equity	72,284	105,310
Lease liabilities	1,616	0
Non-current liabilities	1,616	0
Trade payables	2,394	5,054
Lease liabilities	847	0
Other short-term liabilities	3,020	4,500
Current liabilities	6,261	9,554
Total equity and liabilities	80,161	114,864

Unaudited consolidated statement of cash flows

In '000 euro (for the period ended on June 30)	2019	2018
Cash flows from operating activities		
Loss for the period	-33,311	-15,171
Finance expense	175	74
Finance income	-236	-571
Depreciation of property, plant and equipment	600	256
Amortization and impairment of intangible assets	18,468	1,577
Equity settled share-based payment transactions	257	-52
Decrease in trade and other receivables including tax receivables and inventories	1,036	-258
Decrease in short-term liabilities	-4,140	-10,560
Net cash flows used (-) in operating activities	-17,151	-24,706
Cash flows from investing activities		
Disposal of property, plant and equipment (following a sale)	14	58
Decrease / Increase (-) in investments	0	23,915
Interest received and similar income	44	90
Purchase of property, plant and equipment	-73	-88
Purchase / divestment (-) of other non-current assets	0	-1
Net cash flows used (-) / generated in investing activities	-15	23,974
Cash flows from financing activities		
Restricted cash reserved for issue of share capital	0	10,000
Principal paid on lease liabilities	-407	0
Interest paid on lease liabilities	-13	0
Paid interests	-4	-4
Net cash flows used (-) / generated in financing activities	-424	9,996
Net change in cash and cash equivalents	-17,590	9,265
Net cash and cash equivalents at the beginning of the period	64,652	66,175
Effect of exchange rate fluctuations	63	353
Net cash and cash equivalents at the end of the period	47,125	75,793

Unaudited consolidated statement of changes in equity

	Share capital	Share premium	Cumulative translation differences	Other reserves	Retained earnings	Attributable to equity holders of the company	Non-controlling interest	Total
As at January 1, 2018	151,991	157,661	-335	-13,141	-163,546	132,630	727	133,357
Loss for the period 2018	0	0	0	0	-15,028	-15,028	-143	-15,171
Change to foreign currency translation difference and revaluation reserve	0	0	-58	0	0	-58	0	-58
Capital increase	9,796	204	0	0	0	10,000	0	10,000
Capital decrease	-24,302	-157,865	0	0	182,167	0	0	0
Share-based payment transactions	0	0	0	-52	0	-52	0	-52
As at June 30, 2018	137,485	0	-393	-13,193	3,593	127,492	584	128,076
As at January 1, 2019	137,564	13	-273	-12,563	-19,853	104,888	422	105,310
Loss for the period 2019		0	0	0	-33,317	-33,317	6	-33,311
Change to foreign currency translation difference and revaluation reserve		0	29	0	0	29	0	29
Share-based payment transactions		0	0	256	0	256	0	256
As at June 30, 2019	137,564	13	-244	-12,307	-53,170	71,856	428	72,284