2022 ANNUAL REPORT

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Nicox S.A.

A French public limited company (*société anonyme*) with share capital of €50,156,698
Registered Office: 2405, route des Dolines
06560 Valbonne Sophia Antipolis
France
R.C.S. No. 403 942 642 Grasse

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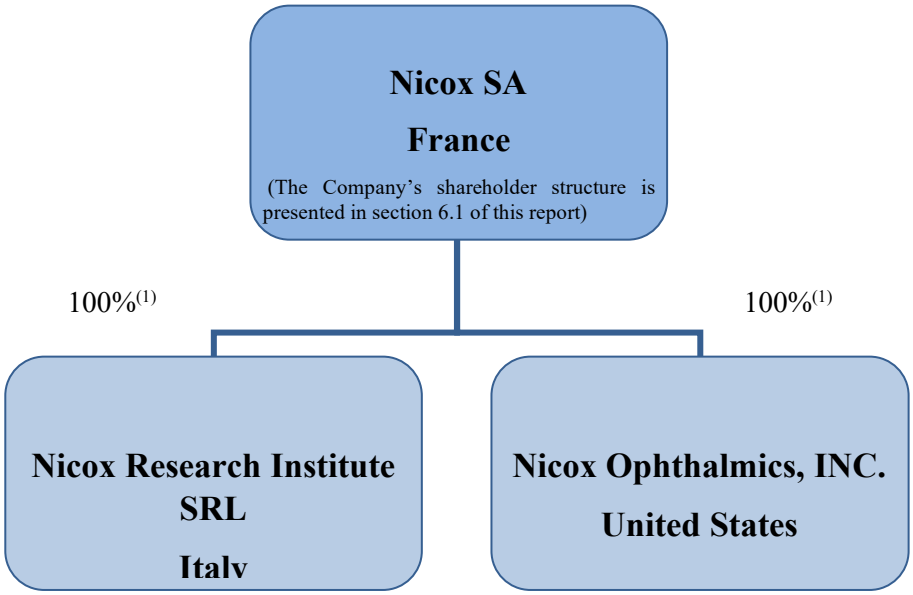
Organization chart



(1) Percentage of capital and voting rights

Information about the Company

Nicox SA

Drakkar 2 – Bât D
2405 route des Dolines
Sophia Antipolis – 06560 Valbonne – France

Nicox SA is registered at the "*registre du commerce et des societies*" (Company Register) of Grasse, France, (Postal code 06133) under the number 403 942 642. The Nicox SA APE code is 7211Z.
LEI code: 969500EZGEO9W4JXR353

Nicox SA is the Group's parent company, incorporated on February 27, 1996, and has been listed on the Euronext Growth Paris (ALCOX) since April 28, 2023. Prior to that, the Company was listed on Euronext Paris (COX.PA) since November 3, 1999. The headquarters is located in Valbonne Sophia Antipolis, France and includes the Finance, Legal, Corporate Development, Communications and Investor Relations departments. Nicox has two international subsidiaries, one in North Carolina, United States, focused on development, the other in Milan, Italy, focused on research and non-clinical development. Both these subsidiaries are consolidated.

At December 31, 2022, Nicox had 28 employees, including teams supporting development operations in the United States and research activities and pre-clinical development in Italy.

List of the Company's subsidiaries

Nicox Ophthalmics Inc.

4819 Emperor Blvd
Suite 400, Durham
NC 27703 – United States

Nicox Ophthalmics Inc. was created on September 25, 2007 and is devoted to clinical development. The development team has an in-depth experience in chemistry, manufacturing and controls (CMC) and clinical development, with a strong focus in ophthalmology. They work with experienced and leading contract manufacturing and clinical research organizations to conduct our clinical studies.

Nicox Research Institute Srl

Via Ludovico Ariosto, 21
20091 Bresso – Milan – Italy

Nicox Research Institute Srl, incorporated on September 21, 1999, is the Company's non-clinical research and development center with a team of scientists with significant expertise in the synthesis and biological testing of nitric oxide (NO)-donating molecules and in the early development of new molecular entities. The team works through collaborations with high-quality contract research organizations and universities throughout the world, and also manages the extensive Nicox patent portfolio.

Information on holdings

See note 28 to the consolidated financial statements and note 2.23 to the annual financial statements in Parts 3 and 4 of this Annual Report.

1.2. Group activities

1.2.1. Summary of the main activities of the Company

We are an international ophthalmology company developing innovative solutions to help maintain vision and improve ocular health. Nicox has one program in Phase 3 clinical development for glaucoma (the first Phase 3 trial has been completed and the second one is ongoing), a candidate in a preclinical development stage for retinal conditions a product candidate at a development stage with a licensed partner for dry eye disease for the Chinese market. Our pipeline also includes two out-licensed commercialized products with exclusive partners.

- NCX 470, a novel nitric oxide bimatoprost eye drop, is currently in Phase 3 clinical development for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. Mont Blanc, the first of the two Phase 3 clinical trials, has been completed and the results announced in October 2022. The second Phase 3 clinical trial, Denali, is ongoing, and the results are expected in 2025. Mont Blanc and Denali have been designed to fulfill the regulatory requirements for safety and efficacy Phase 3 trials to support NDA submissions in

the U.S. and China. Two new Phase 3b clinical trials to evaluate the dual mechanism of action (NO and prostaglandin analog) in IOP lowering and the potential retinal benefits of NCX 470 are planned to start in H1 2023. We are exploring commercial partnerships for NCX 470 in both the U.S. and Japanese markets. NCX 470 is exclusively licensed to Ocumension Therapeutics in the Chinese and Southeast Asian markets.

- NCX 1728, an NO-donating phosphodiesterase-5 (PDE5) inhibitor, is the lead compound of a new class of NO-donating molecules based entirely on NO-mediated activity. NCX 1728 is currently under preclinical evaluation for development in retinal conditions.

- NCX 4251, a novel and patented ophthalmic suspension of fluticasone propionate nanocrystals, is currently in clinical development stage for patients with dry eye disease. The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, providing long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. We are exploring development partnership for NCX 4251 in the U.S. NCX 4251 is exclusively licensed to Ocumension Therapeutics in the Chinese market.

- VYZULTA®, indicated for the reduction of IOP in patients with open angle glaucoma or ocular hypertension, is exclusively licensed worldwide to Bausch + Lomb. VYZULTA is commercialized in more than 15 countries, including the U.S. and is also approved in a number of other countries.

- ZERVIATE®, indicated for the treatment of ocular itching associated with allergic conjunctivitis, is commercialized in the U.S. by our exclusive U.S. licensed partner Eyevance Pharmaceuticals, a wholly owned subsidiary of Santen Pharmaceutical Co., Ltd. Our exclusive Chinese partner for the development and commercialization of ZERVIATE in China and in the majority of Southeast Asia, Ocumension Therapeutics, has completed a Phase 3 clinical trial in China. Ocumension has submitted a New Drug Application (NDA) for the Chinese market in April 2023. The NDA has been included in the priority review and approval process of National Medical Products Administration of the People's Republic of China ("NMPA"). This will accelerate the approval process and launch of ZERVIATE expected in China in 2024. ZERVIATE is also exclusively licensed for development and commercialization in other territories.

Our lead product candidate, NCX 470, leverages the same technology as VYZULTA, our product commercialized under license, which leverages our proprietary expertise in generating novel patentable molecules and are new molecular entities (NMEs) that release NO. NO is a well-known, small, naturally occurring signaling molecule, plays a key role in the regulation of intraocular pressure, or IOP through activation of an intracellular enzyme, soluble guanylate cyclase (sGC). NO, present in ocular tissues. An NO-donating moiety can be linked to other pharmaceutical agents to improve IOP lowering efficacy. Release of NO and the subsequent activation of sGC is one of the mechanisms that is believed to lead to IOP lowering by Nicox's novel molecules. Adding NO to well-known molecules, such as prostaglandin analogs (PGAs), which is the most commonly prescribed class of IOP-lowering drugs, adds a potential second mechanism of action (MOA), and we believe allows certain of our products and product candidates to lower IOP further than the parent molecule

alone. We believe that by designing our proprietary molecules with a dual MOA, we may be able to achieve greater IOP lowering compared to the parent compound alone. As well, the addition of the NO moiety likely changes the properties of the PGA alone allowing the dosing of a higher concentration of the PGA without the proportional increase in associated side effects.

Product candidates

- NCX 470, developed based on our internally developed NO-donating research platform, is our lead product candidate. NCX 470, an NME, is a novel nitric oxide bimatoprost eye drop formulated as an ophthalmic solution, which is currently in Phase 3 clinical development for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. The first Phase 3 trial, Mont Blanc, a multi-regional, double-masked, 3-month, parallel group trial, which evaluated the efficacy and safety of NCX 470 ophthalmic solution, 0.1% compared to latanoprost ophthalmic solution, 0.005% for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension, has been completed and the results announced in October 2022. In Mont Blanc, NCX 470 achieved the primary objective of non-inferiority in lowering IOP compared to the standard of care, latanoprost and met the efficacy requirements for approval in the U.S. However, the secondary efficacy, statistical superiority to latanoprost, was not achieved. NCX 470 was statistically superior to latanoprost in intraocular pressure reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6 timepoints. NCX 470 is the first non-combination product to demonstrate statistical non-inferiority to a prostaglandin analog in a pivotal trial. A second Phase 3 clinical trial, Denali similarly designed to Mont Blanc, is currently being jointly conducted and equally financed at clinical sites in the U.S. and China by Nicox and Ocumension, its exclusive partner for the development and commercialization of NCX 470 in the Chinese, Korean and Southeast Asian markets. The Chinese part of Denali was initiated in December 2021. Denali trial, which includes a long-term safety extension, is expected to randomize approximately 670 patients, at approximately 60 clinical sites in the U.S. and China, with approximately 80% of the patients to be recruited in the U.S and the remaining 20% of the patients to be recruited in China. Denali and Mont Blanc are designed to fulfill the regulatory requirements for Phase 3 safety and efficacy trials to support NDA submissions in the U.S. and China. The results of Denali trial are expected in 2025. This date is based on projections of increased recruitment which take notably into account the lifting of COVID-19 restrictions in China. We are exploring commercial partnerships for NCX 470 in both the U.S. and Japanese markets. NCX 470 is exclusively licensed to Ocumension in the Chinese and Southeast Asian markets.

In the U.S., a multicenter, dose-response, Phase 2 clinical trial, Dolomites, NCX 470 ophthalmic solution 0.065% demonstrated non-inferiority and statistical superiority, based on the trial's pre-specified statistical analysis plan of diurnal mean IOP reduction at Day 28, to latanoprost ophthalmic solution, 0.005%, the U.S. market leader in prostaglandin analog prescriptions. The molecules in VYZULTA and NCX 470, discovered using our research platform, are designed to lower IOP through a dual MOA, which combines NO donation, that activates sGC, with PGAs that activate Prostaglandin F, or FP, receptors, to increase the compounds' ability to lower IOP relative to the parent active compounds. In NCX 470, our NO-donating research platform was applied to add an NO-donating group to bimatoprost. Bimatoprost (known by the brand name LUMIGAN) is a PGA and is the current market leader by sales value among all glaucoma therapies in the U.S. and EU, the two largest glaucoma markets worldwide. NCX 470's potential dual MOA is believed to lower IOP by increasing the outflow of fluid from the eye through the primary, or conventional outflow route via trabecular meshwork as well as through secondary, or unconventional outflow route via uveoscleral pathway.

The primary outflow is believed to be increased by NO released from NCX 470 via activation of sGC and relaxation of trabecular meshwork while the secondary outflow pathway is believed to be increased by bimatoprost released from NCX 470 activation of FP receptors. In addition, exploratory studies on NCX 470 in a nonclinical model of retinal cell damage induced by endothelin-1 (ET-1) investigated the potential protective effects of NCX 470 on the retina and the optic nerve head. The results suggest that NCX 470 improves ocular perfusion and restores retinal function in damaged eyes compared to vehicle and therefore may have therapeutic properties in addition to lowering of IOP.

- NCX 1728, NO-donating phosphodiesterase-5 (PDE5) inhibitor, is the lead compound of a new class of NO-donating molecules in which the NO-mediated effects are enhanced and prolonged by concomitant PDE5 inhibition in the same molecule. PDE5 inhibition has been shown to enhance the efficacy and the duration of NO-mediated effects. This class of molecules has the potential to be developed for retinal conditions. NCX 1728 is currently under preclinical evaluation for development in retinal conditions.

Out licensed Product candidate and Products

- NCX 4251, our novel patented ophthalmic nanocrystals suspension of fluticasone propionate, is under development as a topical treatment, applied to the eyelid margins via a unique mode of administration for patients with dry eye disease. Fluticasone propionate, the active ingredient in NCX 4251, is a well-established corticosteroid which has been marketed for more than 20 years for a number of non-ophthalmic indications, including asthma and allergic rhinitis. Fluticasone propionate has an affinity for the glucocorticoid receptor approximately ten times greater than dexamethasone, a corticosteroid commonly used in ophthalmology. Fluticasone propionate has not been approved previously for topical ophthalmic use. Once-daily NCX 4251 0.1% was evaluated in the Mississippi Phase 2b clinical trial, versus placebo in patients with acute exacerbations of blepharitis. The primary outcome measure in the Mississippi trial was the proportion of patients achieving complete cure in all three hallmark signs and symptoms of blepharitis, eyelid redness, eyelid debris and eyelid discomfort, at Day 15, with two secondary outcome measures focused on signs and symptoms of dry eye. The Mississippi trial did not meet the primary or secondary efficacy endpoints. Following a post hoc analysis of the results suggesting that NCX 4251 is effective in reducing dry eye symptoms in patients with higher severity (moderate to severe) of key signs and symptoms of dry eye and a meeting with the U.S. FDA in early 2022, the development of NCX 4251 is focused on dry eye disease. The Company decided to stop the internal development of NCX 4251 and to seek a partner for development in the U.S. The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, providing long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. NCX 4251 is exclusively licensed to Ocumension in the Chinese market.

- Our product commercialized under license, VYZULTA (latanoprostene bunod ophthalmic solution), 0.024%, represents the first FDA approved drug developed based on our internally developed NO-donating research platform. In VYZULTA, a NO-donating group was linked to latanoprost, the active ingredient in XALATAN, a PGA, structurally related to prostaglandins. PGAs are in a class of molecules used in ophthalmology to lower IOP and are believed to do so by activating FP receptors located on the surface of cells. In the U.S., PGAs

are the first line and the most commonly prescribed pharmacotherapy class for the lowering of IOP in glaucoma and ocular hypertensive patients. VYZULTA is the first PGA with one of its metabolites being NO approved by the FDA for the reduction of IOP. NO is believed to lower IOP by increasing the outflow of fluid from the eye via activation of sGC, a different mechanism from that of PGAs. Thus, VYZULTA is believed to possess a dual MOA in a single molecule. Prior to the FDA approval of VYZULTA, there were no other NO-donating products approved in the U.S for the lowering of IOP. VYZULTA, exclusively worldwide licensed to Bausch + Lomb,is commercialized in more than 15 countries, including the U.S., and is also approved in a number of other countries.

- ZERVIATE (cetirizine ophthalmic solution), 0.24%, our second FDA approved product, is a novel formulation of cetirizine developed and approved for the first time as an eye drop. ZERVIATE, which is indicated for the treatment of ocular itching associated with allergic conjunctivitis, is the first product for the topical treatment of ocular allergies to use cetirizine, the active ingredient in ZYRTEC, a well-established oral antihistamine which has been marketed for over 20 years. We believe that the proven safety and efficacy of oral cetirizine currently recognized by physicians will encourage the adoption of ZERVIATE ophthalmic solution. In 2017, we granted Eyevance exclusive rights to commercialize ZERVIATE in the U.S. and transferred the New Drug Application, to Eyevance. ZERVIATE has been commercialized in the U.S. by Eyevance since March 2020. ZERVIATE has been exclusively licensed for development and commercialization to Ocumension in the Chinese and majority of Southeast Asian Region markets. In February 2022 Ocumension successfully completed a Phase 3 clinical trial in China with ZERVIATE. Subject to any additional data requested by the Chinese National Medical Products Administration of the People's Republic of China (NMPA), this Phase 3 trial, in addition to the data package used by the FDA for ZERVIATE in the U.S., is expected to be sufficient to support a Chinese NDA. In April 2023 Ocumension submitted an NDA for the Chinese market. The NDA has been included in the priority review and approval process of the NMPA. This will accelerate the approval process and launch of ZERVIATE expected in China in 2024. ZERVIATE has also been exclusively licensed to Samil in South Korea and Vietnam, to ITROM in Gulf and Arab markets and to Laboratorios Grin in Mexico.

Ophthalmic Products Market

The current treatment landscape for open-angle glaucoma and ocular hypertension is dominated by two drug classes, topical PGAs and topical beta-blockers, with various combinations introduced over the past 20 years. Since PGAs began to replace topical beta-blockers as the first line of IOP-lowering agents in glaucoma, several have been approved and generic competition in the category is significant. In the U.S., PGAs have now replaced beta-blockers as the first line therapy. At the time of approval in the U.S., VYZULTA was the first eye-drop approved in the past 20 years with a novel approach to reducing IOP. This is a situation which we believe has resulted in a significant demand from eyecare providers for new MOAs to lower IOP in patients with open-angle glaucoma or ocular hypertension.

Allergic conjunctivitis is currently treated by both oral and topical ocular antihistamines, with more serious cases requiring topical, or even oral, corticosteroids. The treatment regimens and molecules are well established and most oral and topical antihistamines, are now available as generics in the U.S. A number of previously prescription-only products are now available without a prescription.

The dry eye disease market comprises of pharmaceutical prescription products for both chronic and short-term use and a significant part of non-prescription artificial tears. The principal mode of pharmaceutical treatment is anti-inflammatory. Some short-term prescription products are used intermittently but often on a regular basis, or as adjunctive therapy in case of acute exacerbations in patients already on chronic treatments. A significant number of generic steroids are available for short term use, and the leading branded chronic treatment (RESTASIS) has just become available as a generic.

Worldwide, the sales of pharmaceutical ophthalmic treatments reached $24.9 billion in 2021 and have grown at an average rate of 5.9% annually since 2017, according to IQVIA Health Analytics. In the U.S. alone, ophthalmology sales reached $9.8 billion in 2021, also growing at an average rate of 5.2% annually since 2017. With respect to our markets of focus, worldwide sales of treatments targeting glaucoma were $5.9 billion, out of the $24.9 billion worldwide market for ophthalmic drugs and sales. In the U.S., sales of treatments targeting glaucoma totaled $2.9 billion in 2021, at an average annual rate of growth of 2.4% since 2017 or 30% of the $9.8 billion total of the U.S. ophthalmic drug market. The U.S. prescription market for dry eye products in 2021 was estimated to be $6.1 million prescriptions for a value of $3.4 billion. Additionally, prescription topical treatments for ocular allergies generated approximately $257 million in the U.S. in 2021, not including substantial sales of non-prescription products.

Main patents

Our intellectual property portfolio for Nicox products and product candidates consists of patents and pending patent applications related to composition of matter, pharmaceutical compositions and methods of use. We have patent protection for VYZULTA in the U.S. (until 2025 which may be subject to extension to 2030. Eligibility for a patent term extension has been agreed by the U.S. Patent and Trademark Office, USPTO, for ZERVIATE (protection in the U.S. until 2030 and 2032, protection in Europe, Japan and Canada until 2030) and for NCX 470 (worldwide protection until 2029 under a composition of matter patent with potential extension up to 5 years in the U.S. and EU and formulation patent until 2039 in the U.S., EU, Japan and China), and for NCX 4251 (worldwide protection by patents until 2033 and to 2040 by additional patents granted in the EU,Japan and China).

1.2.1.1. Our Competitive Strengths

We believe the following key competitive strengths are core to our ability to develop novel treatment solutions for our patients and become a leader in ophthalmology:

- Our clinical stage pipeline, consisting of novel therapies targeting inadequately met or unmet medical needs within ophthalmology, including glaucoma and dry eye disease, in development both internally and with partners;

- Our proven NO-donating research platform, which we believe provides a competitive advantage for the discovery of innovative product candidates for the lowering of IOP, as validated by VYZULTA, the results of the NCX 470 Dolomites (Phase 2) and Mont Blanc (Phase 3) clinical trials;

- Our proven ability to enter into successful partnerships with leading biopharmaceutical companies, as demonstrated by our worldwide exclusive licensing agreement with Bausch + Lomb for VYZULTA, to enter into regional collaboration agreements as demonstrated by the exclusive licensee agreements with Ocumension and to enter into

commercialization partnerships, as demonstrated by our exclusive licensing agreement with Eyevance and as well by the development and commercialization agreements with Ocumension, Samil, ITROM and Laboratorios Grin;

- Our significant experience in ophthalmic drug discovery and development as well as extensive operational, financial and public company experience across both our management team and our board of directors. Our key executives and board members have held leadership roles within major pharmaceutical ophthalmology companies, including divisions of Alcon, Inc., Allergan, Inc., Novartis, ISTA Pharmaceuticals, Inc and Santen Ltd.

1.2.1.2. Our Strategy

We plan to optimize internal resources by advancing the clinical development of our lead asset NCX 470 while seeking a commercial partner for the U.S. and Japanese markets for this product. We also plan to maximize our other assets by entering new other partnerships. We are also considering external growth through strategic transactions. The strategy is subject to obtaining sufficient or additional financing where necessary.

Key elements of our strategy include:

- ***Advance our lead product candidate, NCX 470, in Phase 3 clinical development for open-angle glaucoma and ocular hypertension, through clinical development to approval in the U.S.***

- ***Optimize development through partnerships.*** We are seeking to optimize development and commercialization of our product candidates through regional collaborations where appropriate, to leverage the resources of a partner, such as our partnerships with Ocumension on NCX 470 in the Chinese, Korean and Southeast Asian markets and NCX 4251 in the Chinese market. We are seeking a development partner for NCX 4251 outside the Chinese markets where it is exclusively licensed to Ocumension, and commercial partners for NCX 470 for the U.S. and Japanese markets. In certain instances, we may partner a program for exclusive development;

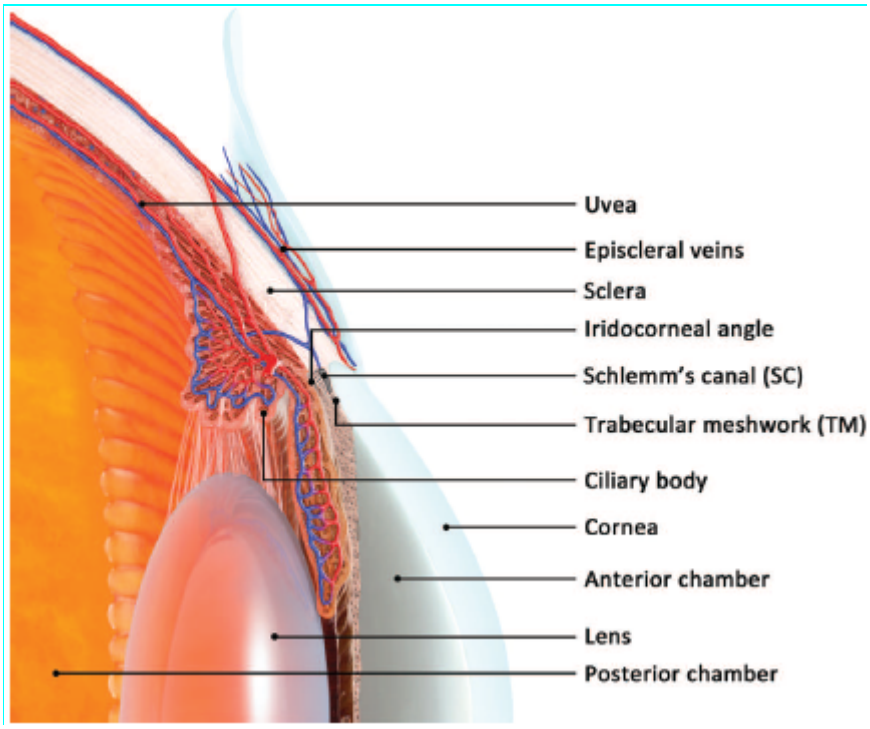
- ***Demonstrate value in our early-stage pipeline.*** Nicox plans to continue pre-clinical evaluation of NCX 1728, an NO-donating PDE5 inhibitor, the lead candidate from a new class of NO-donating molecules based entirely on NO-mediated activity, in retinal conditions;

- ***Evaluate opportunity for pipeline growth*** from external opportunities.

1.2.1.3. Description of the Eye

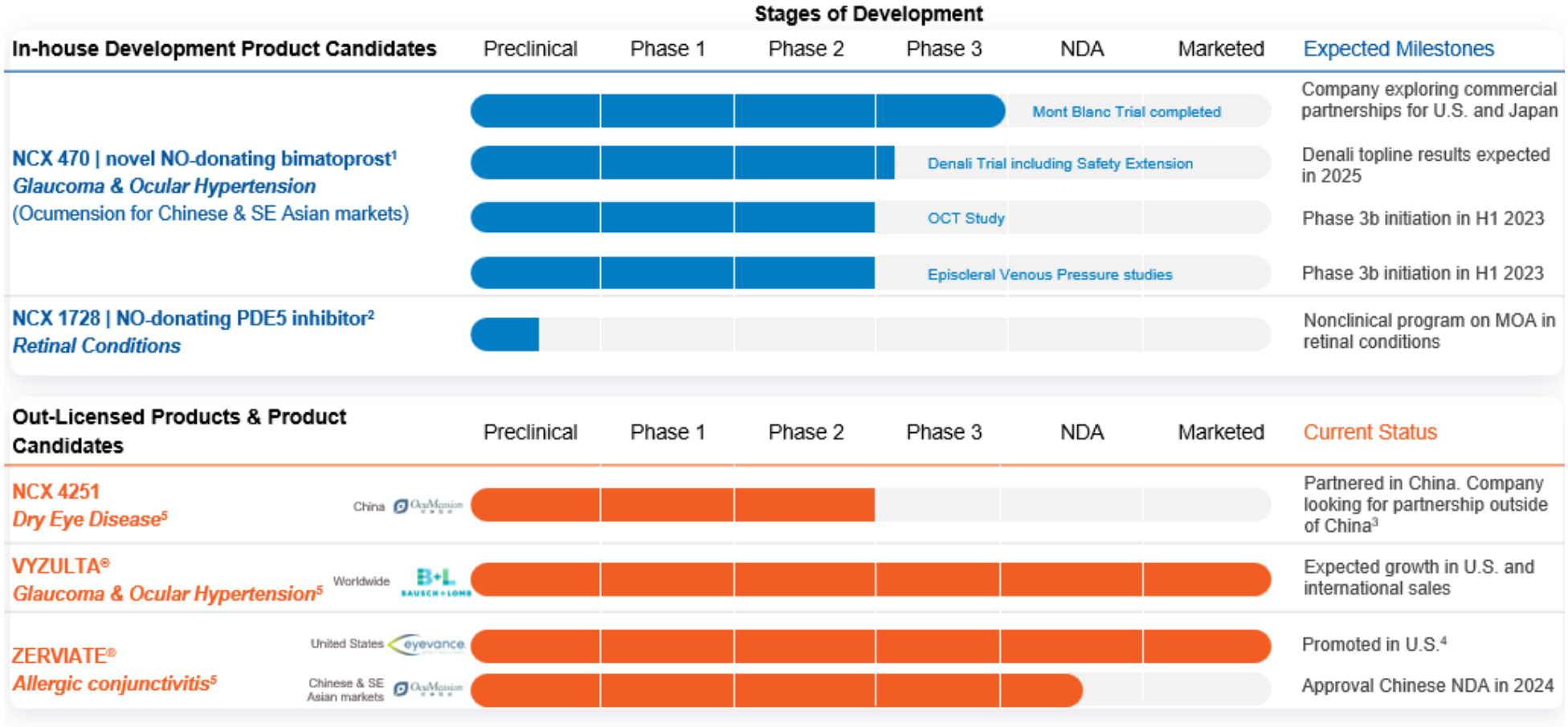
The eye is a fibrous globe that maintains its spherical geometry by being filled with a fluid called aqueous humor on the front side of the eye adjacent to cornea (also called the anterior segment) and a gel called vitreous humor on the back side of the eye adjacent to retina (also called the posterior segment). Both the front of the eye and the back of the eye are at the proper pressure to maintain the eye's shape and thus maintain an unobstructed and optically clear path for the light through the cornea and the lens to the retina. To maintain the pressure in the front of the eye, and therefore its shape, the aqueous humor is constantly produced inside the front compartment of the eye by a tissue known as the ciliary body and flows forward through the pupil and into the angle defined by the front of the iris and the back of the cornea.

Blockages or malfunctions in this drainage system can result in abnormally high IOP often resulting in glaucoma. If left untreated, glaucoma can progress and may lead to irreversible vision loss.



1.2.1.4. Our Pipeline

We believe that our pipeline is strong in glaucoma and broad across eye diseases of the anterior segment (i.e., the front of the eye), with one product candidate in Phase 3 clinical development internally, one product candidate at a development stage with a licensed partner for the Chinese market, a candidate at a preclinical development and two out-licensed commercial products:



1. In addition to our Chinese partner, the Company is actively looking for commercial partners in the U.S. and Japan, to maximize the value of NCX 470. The ongoing Denali trial is not financed beyond the current cash runway of Q22024. New Phase 3b clinical trials and nonclinical studies concerning the dual mechanism of action and the potential beneficial effects of NCX 470 on the retina are planned to report results in the next 12 to 18 months which may strengthen the therapeutic profile of NCX 470. This date is based on projections of increased recruitment which take notably into account the lifting of COVID-19 restrictions in China.
2. Planned costs of nonclinical activities on NCX 1728 are not significant.
3. The net book value of NCX 4251 was decreased to zero (reduction of €15.1 million in 2021 and €11.0 million in H1 2022) in the U.S. due to the additional costs and timings associated with the change in indication, followed by the decision to out-license the product.
4. The net book value of ZERVIATE (€26 million) corresponds mainly to the value of the asset allocated to the Chinese territory, for which the rights were granted to the partner Ocumension. There was an impairment (€12.7 million) to the value in the U.S. in 2021 taking into consideration changes in the U.S. market for topical anti-allergics.
5. The costs of development and commercialization of these products and product candidates are paid by the partner.

Overview

Our product candidate pipeline features clinical and preclinical development stage assets with a potential to address unmet needs in various eye conditions. Those targeting the lowering of IOP in patients with open-angle glaucoma or ocular hypertension and retinal conditions are from our internally developed NO-donating research platform. The pipeline also includes a novel and proprietary formulation of a well-established steroid, that has previously been used in other indications and therapeutic areas, which is under development for dry eye disease.

In addition, we have two commercialized products; VYZULTA, commercialized in more than 15 countries, including the U.S., and also approved in a number of other countries by our exclusive worldwide licensee, Bausch + Lomb, and ZERVIATE, commercialized in the U.S. since March 2020 by our exclusive U.S. partner Eyevance Pharmaceuticals.

Using NO in ophthalmology

We have developed a leading position in the therapeutic application of NO-donating compounds in ophthalmology. Our compounds are designed to release NO with a pharmacological benefit believed to be elicited locally at the tissue level via NO activation of the intracellular enzyme soluble guanylyl cyclase (sGC) expressed within ocular tissues.

NO is a well-known small naturally occurring signaling molecule whose target is an intracellular enzyme, sGC, which converts guanosine triphosphate to the second messenger, cyclic guanosine monophosphate, or cGMP. The cellular machinery, that synthesizes endogenous NO, is present in ocular tissues, together with other components involved in the NO signaling cascade via the activation of sGC. The NO stimulated increase in the concentration of cGMP in the trabecular meshwork leads to the sequestration of intracellular calcium, the relaxation of the trabecular meshwork and, consequently, an increase in the outflow of the aqueous humor from the anterior segment of the eye through the primary or conventional outflow pathway (i.e., via the trabecular meshwork, Schlemm's canal, aqueous veins, and episcleral veins). All of the foregoing events are thought to lead to lowering of IOP. The effect of NO in the sGC signaling cascade may be further increased or prolonged by sGC stimulators, which interact synergistically with NO to increase the production of cGMP. Additionally, the effect of NO on IOP lowering may be further increased and/or prolonged by PDE5 inhibitors, which inhibit the degradation of cGMP. Studies have shown that topical administration of traditional NO donors, such as nitroglycerin or isosorbide mononitrate, reduces IOP, reinforcing the role of NO in IOP regulation. Lower levels of NO markers in aqueous humor are found in open angle glaucoma patients compared to individuals without glaucoma. Several studies conducted in animal models, as well as in glaucoma patients, have shown that the release of NO activates sGC and lowers IOP.

Our lead clinical development product candidate NCX 470, a novel NO-donating bimatoprost eye drop, and our commercialized product with the same mechanism of action, VYZULTA, both release two active metabolites, namely NO and the respective prostaglandin analogs (latanoprost acid for VYZULTA and bimatoprost acid for NCX 470). that observed with the respective parent drugs. By designing our proprietary molecules with a dual MOA, we aim to increase their respective IOP lowering efficacy compared to the molecules acting by a single mode of action. Based on this approach, our partnered approved product VYZULTA, the only NO-donating molecule approved for an ophthalmic indication in the U.S., and our product candidate NCX 470 currently in Phase 3 clinical development has met the primary efficacy objective of non-inferiority in lowering intraocular pressure (IOP) compared to the standard of care, latanoprost 0.005%, in Mont Blanc Phase 3 trial. The results demonstrated that NCX 470 has a robust intraocular pressure lowering effect, with good tolerability. NCX 470 is the first non-combination product to demonstrate statistical non-inferiority, and

numerically greater intraocular pressure reduction compared to a prostaglandin analog in a pivotal trial.

NO-donating research platform

Using our proprietary expertise in generating novel, patentable molecules, which are NMEs that release NO, our research center has conducted lead generation and lead evaluation in preclinical studies in ophthalmology, creating a significant patent portfolio.

We have focused our research efforts on ocular disorders in which NO is believed to play a major role in controlling IOP or retinal health. Our research platform produced the NO-donating compounds, VYZULTA and NCX 470. We are applying key learnings from our research activities to NO-donating moieties attached to other non-PGA therapeutic classes of compounds with the goal of enhancing the NO-mediated effects. NCX 1728, an NO-donating PDE5 inhibitor, is the lead candidate from a new class of NO-donating molecules in which NO-mediated effects are enhanced and prolonged by concomitant phosphodiesterase-5 (PDE5) inhibitory activity within the same molecule. PDE5 inhibition has been shown both to enhance the efficacy and the duration of NO-mediated effects. This novel class of molecules has the potential for development in retinal conditions. NCX 1728 is currently under preclinical evaluation for development in retinal conditions.

Mechanism of action of NO and NO-donating prostaglandin analogs

Evidence suggests that PGAs, which are indicated for reducing elevated IOP in patients with open-angle glaucoma or ocular hypertension, have a MOA which works via prostaglandin FP receptor activation with a primarily positive impact on the activity of certain enzymes, resulting in a widening of the interstitial spaces of the ciliary muscle and contributing to increased uveoscleral outflow of the aqueous humor. This pathway is referred to as the nonconventional or the secondary pathway. However, the conventional or the primary pathway, wherein aqueous humor exits the eye through the trabecular meshwork into Schlemm's canal, a circumferential vessel in the angle of the eye between the cornea and the iris that collects the aqueous humor from the anterior chamber and delivers it to the venous blood vessels, is believed to be a major limiting factor in aqueous humor outflow, and the flow through the primary or conventional pathway is decreased in glaucoma. PGAs may have only a small impact on this pathway.

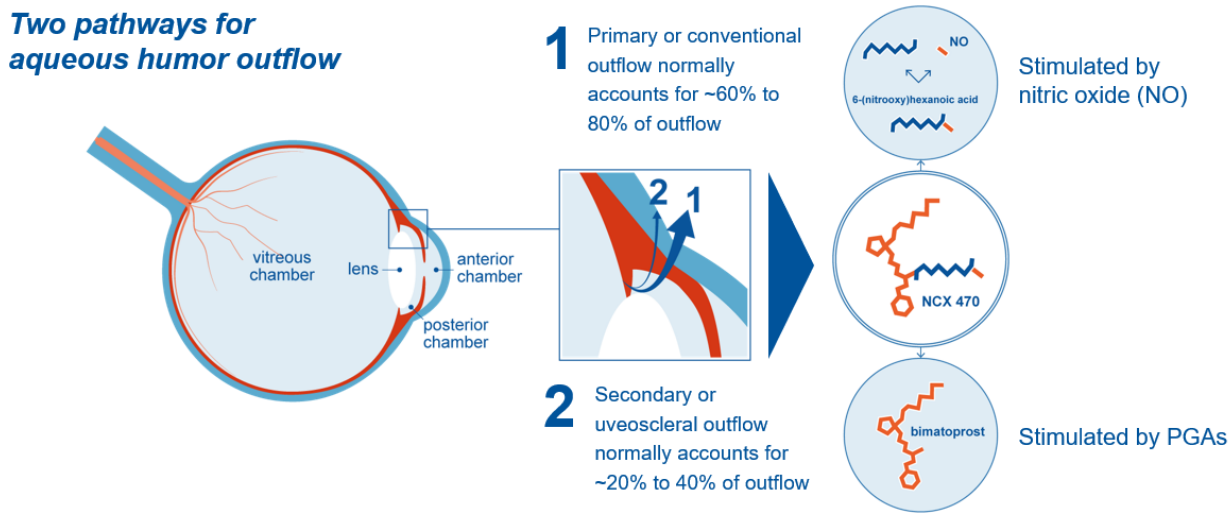
Because the primary or conventional pathway is known to be NO sensitive, we sought to create a compound that would both release a PGA to target the uveoscleral and secondary pathway by activating FP receptors and, at the same time, release NO to stimulate sGC to target the primary or conventional pathway in order to achieve a novel dual MOA. Through investigating this mechanism, latanoprostene bunod was discovered in our research center in Italy. Latanoprostene bunod (the active ingredient in VYZULTA) is an NO--donating version of an existing drug, latanoprost, which belongs to the category of prostaglandin F2alpha analogs. Latanoprostene bunod is metabolized, after application on the ocular surface, into latanoprost acid and another moiety which is then further metabolized to release NO.

The preclinical and clinical data demonstrate that latanoprostene bunod lowers IOP to a greater extent than latanoprost alone in multiple animal models and in glaucoma patients. Our partner, Bausch + Lomb, conducted preclinical studies to investigate the effect of latanoprostene bunod on primary human trabecular meshwork cell contractility to determine whether latanoprostene bunod might mediate this additional IOP lowering through the conventional outflow pathway. Results from these preclinical studies support the concept that latanoprostene bunod has a dual MOA and may target both aqueous outflow pathways to lower IOP in patients with glaucoma or ocular hypertension.

These data have been further supported by results of a Phase 2 clinical trial of latanoprostene bunod versus latanoprost conducted in glaucoma and ocular hypertension patients, and in the subsequent Phase 3 trials which led to approval of the product in the U.S.

As mentioned above, NCX 470 is a novel NO-donating bimatoprost eye drop that releases both NO and bimatoprost, an FDA-approved PGA that is the current U.S. branded market leader by sales marketed under the brand LUMIGAN. NCX 470 is the first non-combination product to demonstrate statistical non-inferiority, and numerically greater IOP reduction, compared to a prostaglandin analog in a pivotal trial. Both NCX 470 and VYZULTA are designed to lower IOP via two MOAs. Upon administration to the eye, NCX 470 and VYZULTA are metabolized in the eye into the PGAs, bimatoprost acid and latanoprost acid, respectively, and the NO-donating moiety. This NO-donating moiety is then further transformed, breaking down into NO and inactive organic compounds. The PGA, one of the active components of NCX 470 and VYZULTA, is released in the eye and is believed to interact with the prostaglandin F2 alpha receptors. This interaction is thought to trigger signaling cascades that ultimately lead to rearrangement of the smooth ciliary muscle in the eye's middle layer, called the uvea, which in turn improves the outflow of the fluid present in the eye, or aqueous humor, from the fluid-filled- chamber at the front of the eye backwards through the uvea and sclera (the white fibrous capsule of the eye). This outflow is referred to as the uveoscleral, unconventional or secondary outflow pathway. NO, the second active component released by NCX 470 and VYZULTA, is thought to enhance the outflow of the eye fluid by the conventional or primary outflow pathway, by modulating the eye tissues called the trabecular meshwork and changing the structure of a canal inside the eye known as Schlemm's canal. The released NO is thought to trigger signals leading to a decrease in cell contractility and volume and, thus, allowing an enhancement of the conventional outflow pathway.

The picture below shows the MOAs of NO-donating PGAs: The trabecular meshwork outflow, also known as the primary or conventional outflow pathway, which is NO sensitive and the uveoscleral outflow, the secondary or non-conventional outflow pathway that is PGA sensitive.



Glaucoma Overview

Glaucoma is a disease of the optic nerve which, if left untreated, can lead to irreversible vision loss. Glaucoma is currently considered to be one of the three leading causes of irreversible blindness worldwide. Glaucoma is frequently linked to elevated intraocular pressure (IOP) and is often due to blockage in drainage system in the front of the eye. Current medications act by reducing IOP to slow the progression of the disease. It is generally accepted that every mmHg of IOP lowering results in a risk reduction disease progression of approximately 10%. Numerous eye drops are available that either decrease the amount of fluid produced in the eye or improve its flow out of the eye. 40% of patients fail to reach target IOP with existing monotherapies, risking disease progression and vision loss. Despite having well established first line therapies, including the standard of care, latanoprost, there remains an unmet need for therapy with a greater IOP-lowering efficacy that is both safe and well tolerated.

High IOP usually does not cause any symptoms, except in cases of acute angle closure in which the IOP may rise to three or four times that of normal IOP and can be painful and can lead to optic nerve damage and vision loss if left untreated. Optic nerve damage and vision loss can also occur in patients with normal IOP, normotensive glaucoma patients, who are also treated with IOP lowering medications. The Normal Tension Glaucoma Study completed in 1998 showed that lowering IOP slowed the progression of normal tension glaucoma, a form of glaucoma in which the patient's IOP is within normal ranges.

In 2021, worldwide sales of treatments targeting glaucoma were $5.9 billion, out of the $24.9 billion worldwide market for ophthalmic drugs. In the U.S., sales of treatments targeting glaucoma totaled $2.9 billion in 2021 or 30% of the $9.8 billion U.S. market for ophthalmic drugs. Of the U.S. sales of treatments targeting glaucoma, $1.3 billion, or approximately 43%, were sales of prostaglandin analogs, of which 80% were branded products led by LUMIGAN with 63% share. Nearly 80% of the PGA prescriptions are for generic latanoprost. PGAs are currently used as the first line standard of care pharmacotherapy in the U.S.

While not derived from head-to-head trials, the table below provides a summary of the U.S. FDA labeling information for the currently used first-line pharmacotherapies.

Summary of the U.S. FDA Labeling Information for the Currently Approved First-line Pharmacotherapies for the Reduction of IOP in Patients with Open-Angle of Glaucoma or Ocular Hypertension.

	XALATAN[1] (latanoprost 0.005%)	**LUMIGAN[1] (bimatoprost 0.01%)**	**TRAVATAN Z[1] (travoprost 0.004%)**	**VYZULTA[2] (latanoprostene bunod 0.024%)**	**ROCKLATAN[1] (latanoprost 0.005% and netarsudil 0.02%)**
IOP reduction	6 to 8 mmHg	Up to 7.5 mmHg (7 to 8 mmHg for 0.03% bimatoprost)	7 to 8 mmHg	Up to 7 to 9 mmHg	6.8 to 9.2 mmHg 1 to 3 mmHg greater than latanoprost or netarsudil (1.58 mmHg greater than latanoprost 0.005% at 3 months)[3]
Patient mean baseline IOP	24 to 25 mmHg	23.5 mmHg (26 mmHg for 0.03% bimatoprost)	25 to 27 mmHg	26.7 mmHg	23.6 mmHg[4]
Adverse reactions	Foreign body sensation 13%; punctate keratitis 10%; stinging 9%; conjunctival hyperemia 8%	Conjunctival hyperemia 31% (45% for 0.03% bimatoprost)	Conjunctival hyperemia 30% to 50%	Conjunctival hyperemia 6%; eye irritation 4%; eye pain 3%; instillation site pain 2%	Conjunctival hyperemia 59%; instillation site pain 20%; corneal verticillata 15%; conjunctival hemorrhage 11%

(1) Indicated for the reduction of elevated intraocular pressure in patients with open angle- glaucoma or ocular hypertension.

(2) Indicated for the reduction of intraocular pressure in patients with open angle- glaucoma or ocular hypertension.

(3) See Section 14, Clinical Studies, Figure 1 and 2 of ROCKLATAN package insert for diurnal IOP at Day 90 for ROCKLATAN vs. Latanoprost including both Mercury-1 and Mercury-2 IOP values (1.5; 1.7; 1.3; 1.5;2.0; and 1.5 mmHg).

(4) See Section 14, Clinical Studies, Figure 1 and 2 of ROCKLATAN package insert for baseline IOP for ROCKLATAN including both Mercury-1 and Mercury-2 IOP values (24.8; 23.7; 22.6; 24.7; 23.3; 22.4 mmHg).

For patients whose glaucoma is not well-controlled on a single PGA eye drop, adjunctive therapies are added on the top of PGAs as second, third and fourth eye drops. The adjunctive therapies include beta blockers, alpha agonists, carbonic anhydrase inhibitors, rho kinase inhibitors, or their fixed dose combinations. As the number of medications increases, compliance decreases and hence the opportunity for more effective single-drop treatments remains. The total sales of adjunctive therapies accounted for approximately $1.6 billion of the $2.9 billion U.S. sales of treatments targeting glaucoma in 2020. Currently, it is estimated that 3.5% of the worldwide population between 40 and 80 years of age are affected by the most common forms of glaucoma, and it is estimated that, in 2020, around 34.5 million prescriptions were written in the U.S. annually for glaucoma drugs.

Product Candidates Pipeline

NCX 470 - Our Lead Product Candidate

NCX 470, an NME, is a novel nitric oxide bimatoprost eye drop currently in Phase 3 clinical development for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. Mont Blanc, the first of the two Phase 3 clinical trials, which evaluated the safety and efficacy of NCX 470 has been completed and the results announced in October 2022. In Mont Blanc NCX 470 achieved the primary objective of non-inferiority in lowering IOP compared to the standard of care, latanoprost and met the efficacy requirements for approval in the U.S. However, the secondary efficacy, statistical superiority to latanoprost, was not achieved. NCX 470 was statistically superior to latanoprost in intraocular pressure reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6 timepoints. NCX 470 is the first non-combination product to demonstrate statistical non-inferiority to a prostaglandin analog in a pivotal trial.

A second, similarly designed, Phase 3 clinical trial, Denali, evaluating NCX 470 is currently being conducted at clinical sites in the U.S. and China.

NCX 470 is designed to release both bimatoprost and NO into the eye to lower IOP by two pathways in patients with open-angle glaucoma and hypertension. Bimatoprost, marketed under the brand name LUMIGAN® by Allergan, Inc., is the leading branded product by sales in the class of PGAs, the most widely used class of drugs for the treatment of IOP-lowering in patients with open-angle glaucoma and ocular hypertension. Bimatoprost is generally considered to be slightly better at lowering IOP than latanoprost.

In December 2018 we entered into an exclusive licensing agreement with Ocumension for the development and commercialization of NCX 470 in the Chinese market. In March 2020 Ocumension's exclusive rights were extended to Korea and Southeast Asian markets. We are exploring commercial partnerships for NCX 470 in both the U.S. and Japanese markets.

Topline Results of the First NCX 470 Phase 3 Clinical Trial Mont Blanc

In October 2022 we announced the results of Mont Blanc, the first Phase 3 clinical trial, a randomized, multi-regional, double-masked, 3-month, parallel group trial that evaluated the efficacy and safety of NCX 470 ophthalmic solution, 0.1% compared to latanoprost ophthalmic solution, 0.005% for the IOP lowering in patients with open-angle glaucoma or ocular hypertension. The 0.1% dose of NCX 470 was selected through an initial adaptive design portion of the trial, which also included the 0.065% dose. Latanoprost is the most widely prescribed first-line therapy for open-angle glaucoma or ocular hypertension. Mont Blanc trial enrolled 691 patients in 56 sites in the U.S. and 1site in China. The primary efficacy objective was based on reduction from baseline in mean time matched IOP at 6 timepoints: 8 AM and 4 PM at week 2, week 6 and month 3.

IOP-lowering effect from baseline was 8.0 to 9.7 mmHg for once of daily dosing of NCX 470 0.1% vs. 7.1 to 9.4 mmHg for latanoprost 0.005% (reduction in time-matched IOP at 8 AM and 4 PM across the week 2, week 6 and month 3 visits).

Non-inferiority of NCX 470 was met vs. latanoprost in the primary efficacy analysis. The upper limit of the 95.1% confidence limit on the difference in the treatment effect between NCX 470 and latanoprost in change from baseline in time matched IOP to the follow-up visits (week 2, week 6, and month 3) was ≤1.5 mmHg and ≤1.0 mmHg at all 6 timepoints.

In a pre-specified secondary efficacy analysis of time-matched change from baseline IOP, NCX 470 was statistically superior ($p<0.049$) to latanoprost in IOP reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6 timepoints but did not reach the overall statistical superiority pre-specified as a secondary efficacy endpoint. The difference in IOP reduction between NCX 470 and latanoprost was up to 1.0 mmHg in favor of NCX 470.

NCX 470 was well tolerated; the most common adverse event was ocular hyperemia in 11.9% of the NCX 470 patients vs. 3.3% of latanoprost patients. There were no ocular serious adverse events and no treatment-related non-ocular serious adverse events. 4.3% of patients on NCX 470 discontinued compared to 5.1% on latanoprost.

Second NCX 470 Phase 3 Clinical Trial Denali Ongoing

In November 2020 Nicox initiated the second, Phase 3 trial in the U.S., Denali, jointly conducted and financed in equal parts by Nicox and Ocumension, our exclusive Chinese license partner. The Chinese part of the trial was initiated in December 2021. Denali, similarly designed to Mont Blanc, is a 3-month Phase 3 trial evaluating the safety and efficacy of NCX 470 ophthalmic solution, 0.1% versus latanoprost ophthalmic solution, 0.005%, for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. The Denali trial, which includes a long-term safety extension through 12 months, is expected to randomize approximately 670 patients, at approximately 60 clinical sites in the U.S. and China, with approximately 80% of the patients to be recruited in the U.S and the remaining 20% of the patients to be recruited in China. The topline results are expected in 2025. This date is based on projections of increased recruitment which take notably into account the lifting of COVID-19 restrictions in China.

The Mont Blanc trial and the Denali trial have been designed to fulfill the regulatory requirements to support NDA submissions in the U.S. and China and will also provide data for other countries accepting the same clinical data package for approval. Both trials are necessary, and certain additional clinical and nonclinical data will also be required, to complete NDA submissions in both the U.S. and China.

NCX 470 additional Phase 3b clinical trials

Two new Phase 3b clinical trials planned to start in H1 2023 will evaluate the dual mechanism of action (NO and prostaglandin analog) in IOP lowering and the potential retinal benefits of NCX 470. The trials will evaluate the effect of NCX 470 on Episcleral Venous Pressure (EVP) and outflow through the trabecular meshwork and on the ocular perfusion via Optical Coherence Tomography (OCT) angiography on retinal vessels. Together, these trials are designed to validate NCX 470's dual mechanism of action in humans and potentially demonstrate some of the beneficial effects on the retina that have been observed in nonclinical models.

Top line Results of the Dolomites NCX 470 Phase 2 Clinical Trial

The randomized, double-masked, dose-response Dolomites Phase 2 trial aimed to determine a concentration of NCX 470 for lowering IOP in patients with open-angle glaucoma or ocular hypertension to advance into further clinical development. The trial enrolled 433 patients across 25 sites in the U.S. Patients were randomized to receive either NCX 470 (0.021%, 0.042% or 0.065%) or latanoprost ophthalmic solution, 0.005% once a day in the evening for 28 days.

All three doses of NCX 470 (0.021%, 0.042%, and 0.065%) met the pre-specified primary efficacy endpoint of non-inferiority to latanoprost for reduction from baseline in mean diurnal IOP at Day 28.

In a pre-specified secondary efficacy analysis for reduction from baseline in mean diurnal IOP at Day 28, the mid and high doses of NCX 470 (0.042% and 0.065%) met the secondary efficacy endpoint of statistical superiority to latanoprost based on the trial's pre-specified statistical analysis plan. Specifically, IOP reduction from baseline in mean diurnal IOP at Day 28 was 7.8 mmHg for the 0.021% dose of NCX 470 (p-value for NCX 470 vs. latanoprost not statistically significant); 8.2 mmHg for the 0.042% dose of NCX 470 (p-value for NCX 470 vs. latanoprost=0.0281); and 8.7 mmHg for the 0.065% dose of NCX 470 (p-value for NCX 470 vs. latanoprost=0.0009), compared with 7.4 mmHg for latanoprost 0.005%. The dose dependent IOP reduction from baseline in mean diurnal IOP at Day 28 showed improved IOP lowering with each incremental concentration of NCX 470 tested, thus creating the potential for additional IOP lowering with a higher concentration of NCX 470.

In additional pre-specified secondary efficacy analyses for reduction from baseline in mean diurnal IOP, NCX 470 (0.065%) met the secondary efficacy endpoint of statistical superiority to latanoprost at Day 7 (p=0.004) and Day 14 (p=0.0174), in addition to Day 28 (p=0.0009; described above). In pre-specified secondary efficacy analyses, the 0.065% dose of NCX 470 showed statistical superiority in IOP lowering as a reduction from baseline at all three time points (8 AM, 10 AM and 4 PM IOPs) on Day 28 compared with latanoprost, with the difference reaching up to 1.4 mmHg (p=0.0214 at 8 AM, p=0.0008 at 10 AM, and p=0.0015 at 4 PM). The IOP lowering effect as reduction from baseline at the three time points (8 AM, 10 AM and 4 PM IOPs) across Day 7, Day 14 and Day 28 ranged from 7.6 to 9.8 mmHg for the 0.065% concentration of NCX 470 compared with 6.3 to 8.8 mmHg for latanoprost. Additionally, at Day 28, 44% of patients dosed with NCX 470 (0.065%) had a 1 mmHg or greater mean diurnal IOP reduction from baseline compared with the mean of 7.4 mmHg for the latanoprost group (p-value not significant); 37% of patients had 2 mmHg or greater reduction (p-value not significant); 27% had a 3 mmHg or greater reduction (p=0.0175); 16% had a 4 mmHg or greater reduction (p-value not significant); and 12% had a 5 mmHg or greater reduction (p=0.0150); compared with the mean for the latanoprost group. Furthermore, greater proportion of patients dosed with NCX 470 (0.065%) achieved a mean diurnal IOP reduction at Day 28 of 40% or greater (p=0.0287), 35% or greater (p=0.0393), 30% or greater (p-value not statistically significant), 25% or greater (p=0.0479) and 20% or greater (p=0.0115), compared with those dosed with latanoprost.

NCX 470 was well tolerated when dosed once daily for 28 days in patients with open-angle glaucoma or ocular hypertension. Only three out of the 433 patients in the trial discontinued due to an adverse event. The majority of adverse events in the trial were mild. The most frequently reported adverse event was conjunctival hyperemia, the majority of which were mild, in 16.8% of patients who dosed with the 0.065% dose of NCX 470 compared with 6.5% of patients who dosed with latanoprost. Notably, adverse events for conjunctival hyperemia plateaued at the 0.042% concentration, for which it was reported for 22.2% of patients. There were no treatment-related serious adverse events, and no evidence of treatment-related systemic side effects.

NCX 470 nonclinical studies

In rabbit, dog and nonhuman primate nonclinical models of IOP, our data demonstrate that NCX 470 is able to lower IOP more than bimatoprost alone, with up to 3.5 mmHg greater lowering of IOP with NCX 470 as compared with bimatoprost 0.03% in a non-human primate model when tested with equimolar solutions (or solutions containing equivalent numbers/concentrations of molecules). Additionally, and notably, in the nonclinical model of ocular hypertension in rabbits in which bimatoprost is known not have an effect on IOP, NCX 470 appeared to lower IOP, with up to 8.4 mmHg IOP lowering due to NO alone, suggesting that its NO-donating part of the molecule produces an IOP lowering- action.

NCX 470 exploratory nonclinical studies

Exploratory studies on NCX 470 in a nonclinical model of retinal cell damage induced by endothelin-1 (ET-1) investigated the potential protective effects of NCX 470 on the retina and the optic nerve head. The results suggest that NCX 470 improves ocular perfusion and retinal function in damaged eyes compared to vehicle and therefore may have therapeutic properties in addition to lowering of IOP.

Nonclinical experiments were performed to determine the effect of NCX 470 on ocular vascular reactivity and retinal function after repeated topical ocular dosing in a well-defined model of ischemia/reperfusion injury to the optic nerve in rabbits induced by ET-1. ET-1 alone was administered twice-weekly for 2 weeks, followed by concomitant dosing with NCX 470 or vehicle for a further 4 weeks. Twice-weekly dosing with ET-1 increased ophthalmic artery resistivity after 2 weeks ($p<0.05$ vs. baseline), and the resistivity continued to increase during the next 4 weeks up to approximately 40% of baseline at week 6 in animals treated with ET-1 and vehicle. This detrimental effect was significantly reversed in eyes where ET-1 was co-administered with NCX 470 0.1% twice daily ($p<0.05$ vs. vehicle at week 6). In addition, ET-1 dosing resulted in a marked decline in photoreceptor responses, which continued in eyes treated with vehicle. The decline was almost completely reversed by week 6 in eyes treated with NCX 470 ($p<0.05$ vs. vehicle). These effects are only partially shared by bimatoprost administered at the commercial dose (Lumigan 0.01% ophthalmic solution) or at equimolar doses as that released by NCX 470.

NCX 1728 - Lead compound in a new class of NO-donating molecules based on NO-mediated activity.

NCX 1728, an NO-donating PDE5 inhibitor, is the lead compound of a new class of NO-donating molecules in which the NO-mediated effects are enhanced and prolonged by concomitant PDE5 inhibition within the same molecule. PDE5 inhibition has been shown to enhance the efficacy and the duration of NO-mediated effects. This class of molecules has the potential to be developed for retinal conditions. NCX 1728 is currently under preclinical evaluation for development in retinal conditions.

Out-Licensed Products and Product Candidate

NCX 4251

NCX 4251, which leverages an established molecule, is a novel patented ophthalmic suspension of fluticasone propionate nanocrystals in development as a topical treatment for patients with dry eye disease with a unique mode of application to the eyelid margins via an applicator minimizing the potential steroid exposure through the cornea which can lead to damaging side effects such as intraocular pressure increase found with current topical steroids. NCX 4251 has been evaluated in a Phase 2 trial, Danube, and a larger Phase 2b trial, Mississippi, both of which studied patients with blepharitis. The primary outcome measure in the Mississippi trial was the proportion of patients achieving complete cure in all three hallmark signs and symptoms of blepharitis, eyelid redness, eyelid debris and eyelid discomfort, at Day 15, with two secondary outcome measures focused on signs and symptoms of dry eye disease. Mississippi trial did not meet the primary or secondary efficacy endpoints, Following the *post hoc* results from the Mississippi trial and a subsequent meeting with the U.S. FDA, the future development of NCX 4251 is focused on dry eye disease.

Fluticasone propionate, the active ingredient in NCX 4251, which has not been approved previously for topical ophthalmic use, has an affinity for the glucocorticoid receptor which is approximately ten times greater than dexamethasone, a corticosteroid commonly used in ophthalmology. Fluticasone is a

glucocorticoid with potent anti-inflammatory- properties that has been approved in numerous drug products over the past 20 years for the treatment of various indications including dermatology, rhinitis, and asthma.

In the first half of 2022, the Company decided to stop the internal development of the product candidate and to seek a partner to develop it in the U.S, as the development plan for NCX 4251 is not financed.

The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, providing long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S.

In the event that the Company finds a partner to pursue the development of NCX 4251 in the U.S., the regulatory approval for NCX 4251 using the FDA's Section 505(b)(2) regulatory pathway, similar to ZERVIATE, would be the procedure to follow because it would enables us to rely, in part, on the FDA's prior findings of safety and efficacy for fluticasone propionate, or published literature, in support of our NDA.

In July 2019, we entered into an exclusive license agreement with Ocumension for the development and commercialization of NCX 4251 for blepharitis in the Chinese market. We are exploring a development partnership for NCX 4251 in the U.S.

Dry eye disease

Dry eye disease is a common condition that occurs when the quality and/or quantity of tears aren't able to adequately hydrate or lubricate the eyes. This inadequate lubrication can lead to dryness, inflammation, pain, discomfort, irritation, diminished quality of life, and in severe cases, permanent vision impairment.

The dry eye market consists of both chronic and short-term use prescription products and a significant part of non-prescription products, principally artificial tears. The U.S. prescription market for dry eye products in 2021 was estimated to be 6.1 million prescriptions for a value of $3.4 billion. Around 34 million adults are estimated to be suffering from dry eye disease in the U.S. alone.

The net book value of NCX 4251 was decreased to zero (reduction of €15.1 million in 2021 and €11.0 million in H1 2022) in the U.S. due to the additional costs and timings associated with the change in indication, followed by the decision to out-license the product.

Mississippi Phase 2b Clinical Trial

Nicox completed the Mississippi Phase 2b clinical trial which evaluated the QD dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, against vehicle in patients with acute exacerbations of blepharitis. 224 patients were recruited from 8 clinical sites in the U.S. Patients completed 2 weeks of treatment and two weeks of follow-up. The primary outcome measure was the proportion of patients achieving complete cure in all the three hallmark signs and symptoms of blepharitis, eyelid redness, eyelid debris and eyelid discomfort, at Day 15, with two secondary outcome measures focused on signs and symptoms of dry eye disease.

Mississippi Phase 2b Clinical Trial results in Blepharitis

The Mississippi clinical trial results were announced in September 2021. The Mississippi Phase 2b clinical trial did not meet the primary or secondary efficacy endpoints. However, a signal of NCX 4251's potential efficacy was seen in the trial with NCX 4251 0.1% showing a numerical improvement over vehicle in the primary outcome measure of complete cure in eyelid redness, eyelid debris and eyelid discomfort at Day 15. NCX 4251 also showed a statistically significant difference against placebo in the exploratory endpoint of change from baseline in the composite score of the same key signs and symptoms at Day 8 (p=0.03), Day 11 (p=0.01) and Day 15 (p=0.01). NCX 4251 was found to be safe and well-tolerated over 14 days' treatment, with no serious adverse events, and all of the adverse events for the NCX 4251 treatment arm were mild. There were no discontinuations in the study due to an adverse event.

Mississippi Phase 2b Post-hoc Results in Dry Eye Disease

Positive post hoc results from the Mississippi Phase 2b clinical trial suggest that QD dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, is effective in reducing dry eye symptoms in a subgroup of patients. The post hoc analyses identified a subgroup of patients (123 of 224 patients) with baseline scores ≥2.0 on a scale of 0 (none) to 4 (severe) for inferior cornea fluorescein staining, a key sign of dry eye disease. In this patient group, the analysis demonstrated a statistically significant difference against vehicle for change from baseline in eye dryness scores as assessed on a Visual Analog Scale at Day 8 (p=0.0085), Day 11 (p=0.0020) and Day 15 (p<0.0016). Statistically significant differences against placebo were also observed in other symptoms of dry eye disease (photophobia, blurred vision, burning/stinging, foreign body sensation, ocular itching, pain) at all timepoints during treatment (Day 8, Day 11 and Day 15). In some symptoms the effects persisted up to two weeks after the end of treatment. At Day 15, the difference in reduction from baseline in inferior cornea fluorescein staining reached a p-value of 0.0524, which we believe could reach statistical significance with a larger patient population.

Top-line Results of the Danube Phase 2 Clinical Trial

In December 2019 we completed the U.S. multi-center, randomized, double-masked, placebo-controlled, first-in-man administration, dose-escalation, 14-day Phase 2 clinical trial, Danube, aimed to evaluate the safety and tolerability of NCX 4251 compared to vehicle in patients with acute exacerbations of blepharitis. The trial enrolled 36 patients in clinical sites in the U.S. The Danube Phase 2 trial met the primary objective of selecting the dose of NCX 4251 for further development.

NCX 4251 0.1% once daily (QD) treatment was selected to advance into a larger Phase 2 clinical trial.

The selected dose also demonstrated promising efficacy against exploratory endpoints in the study in reducing the signs and symptoms of dry eye disease.

Danube Phase 2 Clinical Trial Summary

All patients in the once daily (n=10 for NCX 4251 and n=5 for vehicle) and twice daily (n=10 for NCX 4251 and n=11 for vehicle) cohorts successfully completed the 14-day dosing period followed by a 14-day safety evaluation period.

Both once daily (QD) and twice daily (BID) NCX 4251 0.1% were well tolerated. There were no serious adverse events, no treatment related systemic adverse events, and no adverse events of IOP elevation, the most common side effect of topical ophthalmic steroids.

Although the study was not powered for efficacy, in the prospectively defined pooled analysis of QD and BID dosing of NCX 4251 0.1%, there was a statistically significant reduction in the composite score of eyelid redness, eyelid debris and eyelid discomfort at the Day 14 study endpoint (n = 20 for NCX 4251 0.1% and n = 16 for vehicle with p = 0.047 for study eyes and p = 0.025 for the combined study eyes and contralateral eyes). Twenty percent of patients on QD dosing of NCX 4251 achieved complete cure, compared to 0% in patients treated with placebo. Due to the small sample size, these results were not statistically significant. Complete cure was defined as a score of zero in eyelid redness, eyelid debris and eyelid discomfort, also referred to as a Composite Score of zero.

Exploratory analyses of signs and symptoms of dry eye disease, including symptom evaluation using visual analog scale and sign evaluation based on corneal and conjunctival fluorescein staining, revealed encouraging reduction from pre-study baselines.

VYZULTA®

Overview

VYZULTA (latanoprostene bunod ophthalmic solution), 0.024% is a PGA with one of its metabolites being NO. At the time of its approval, VYZULTA was the first eye drop approved in twenty years with a novel approach to reduce IOP. VYZULTA was approved by the FDA in November 2017 for the reduction of IOP in patients with open angle- glaucoma or ocular hypertension. Bausch + Lomb, a leading eye health company, has exclusive worldwide rights to develop and market VYZULTA which is commercialized in more than 15 countries, including the U.S., and also approved in a number of other countries. Other launches are expected in 2023 and beyond.

VYZULTA has demonstrated greater IOP lowering at many of the trial's timepoints, and a comparable safety profile compared with two currently available medications for the lowering of IOP in open angle- glaucoma or ocular hypertension in one Phase 2 clinical trial (compared to latanoprost), and two Phase 3 clinical trials (compared to timolol), respectively.

We believe there is an inadequately met or unmet medical need for products with increased IOP lowering in the glaucoma market. We believe that VYZULTA offers a differentiated treatment based on:

- **Increased IOP Lowering:** In the Phase 3 clinical trials, VYZULTA dosed once daily demonstrated statistically significantly greater IOP lowering than twice daily dosed timolol maleate ophthalmic solution 0.5% throughout the day at three months of treatment. Based on analysis of the pooled results of these trials, the IOP lowering from baseline was in the range of 7.5-9.1 mmHg across three months of treatment. Additionally, in the open-label safety extensions for both Phase 3 trials, VYZULTA demonstrated sustained IOP-lowering effect without any loss of efficacy over 12 months (12-month duration of treatment in first Phase 3 trial and 6-month duration of treatment in the second Phase 3 trial). In the 413 subject Phase 2 randomized trial, VYZULTA demonstrated statistically significantly greater IOP lowering than latanoprost ophthalmic solution, 0.005% after four weeks of treatment. VYZULTA, the 0.024% dose (N=83), showed statistically significant $p<0.01$ greater day time IOP lowering from baseline compared with latanoprost at a dose of 0.005% at day 28, with the difference for VYZULTA reaching greater than 1 mmHg (statistical significance: $p<0.01$).

- **Novel Dual Mechanism of Action:** VYZULTA is the first PGA approved by the FDA for the lowering of IOP with one of its metabolites being NO and the only QD single agent

IOP- lowering- product to provide activity through two potential distinct MOAs that are mediated by a prostaglandin and NO.

- **Established Tolerability Profile:** In the Phase 3 clinical trials, 562 patients were exposed to the drug. VYZULTA administered once a day in the evening was well tolerated with no serious adverse events. The most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%).

With VYZULTA, as with other PGAs, increased pigmentation of the iris and eyelid can occur with iris pigmentation likely to be permanent. Gradual changes to eyelashes, including increased length, increased thickness and number of eyelashes, can occur and are usually reversible upon discontinuation of treatment. The most common ocular adverse reactions are conjunctival hyperemia, eye irritation, eye pain and instillation site pain.

ZERVIATE®

Overview

ZERVIATE, the brand name for our cetirizine ophthalmic solution, 0.24%, is a novel formulation of cetirizine developed and approved for the first time for topical application in the eye. Cetirizine, the active ingredient in ZYRTEC, is a second-generation antihistamine (H1 receptor antagonist) that binds competitively to histamine receptor sites. Cetirizine, in approved oral formulations, has a well characterized- systemic efficacy and safety profile with world-wide exposure resulting from 20 years of oral use. ZERVIATE is the first and only eye drop formulation of the antihistamine cetirizine. In May 2017, the U.S. FDA approved the NDA for ZERVIATE for the treatment of ocular itching associated with allergic conjunctivitis.

In September 2017, we entered into an exclusive licensing agreement with Eyevance for the commercialization of ZERVIATE in the U.S. which is commercialized there since March 2020.

In March 2019 we entered into an exclusive licensing agreement with Ocumension for the development and commercialization of ZERVIATE in the Chinese market. In March 2020 the exclusive rights were expanded to the majority of Southeast Asian markets. Ocumension successfully completed a Phase 3 clinical trial of ZERVIATE in China in February 2022. ZERVIATE was found to be statistically non-inferior to emedastine difumarate, an antihistamine marketed under the brand name EMADINE®. Subject to any additional data requested by the Chinese National Medical Products Administration of the People's Republic of China (NMPA), this Phase 3 trial, in addition to the clinical data package used by the FDA for ZERVIATE in the U.S., is expected to be sufficient to support a Chinese NDA for approval to commercialize ZERVIATE in China. Ocumension has submitted an NDA for the Chinese market in April 2023 which has been included in the priority review and approval process of the NMPA. This will accelerate the approval process and launch of ZERVIATE expected in China in 2024.In December 2019 we entered into an exclusive licensing agreement with Samil for the development and commercialization of ZERVIATE in South Korea. This agreement was expanded to include Vietnam in February 2022.

In August 2020 we entered into an exclusive licensing agreement with ITROM for the registration and commercialization of ZERVIATE in Gulf and Arab markets.

In May 2021, we signed an exclusive license agreement with Laboratorios Grin for the registration and commercialization of ZERVIATE in Mexico.

The efficacy of ZERVIATE was established in three Phase 3 trials that were randomized, double-masked, placebo--controlled-, conjunctival antigen challenged trials in patients with a history of allergic conjunctivitis. Onset and duration of action were evaluated in two of these trials, and patients treated with ZERVIATE demonstrated statistically and clinically significantly less ocular itching compared to its vehicle at 15 minutes and eight hours after treatment ($p<0.05$).

Regulatory approval for ZERVIATE was obtained via the FDA's Section 505(b)(2) regulatory pathway, which enabled us to rely, in part, on the FDA's prior findings of safety and efficacy for cetirizine and the published literature in support of our NDA.

In seven clinical trials conducted in patients with allergic conjunctivitis or those at risk of developing allergic conjunctivitis, the most commonly reported adverse reactions occurred in approximately 1% to 7% of patients treated with either ZERVIATE or vehicle. These reactions were ocular hyperemia, instillation site pain and reduced visual acuity.

About Allergic Conjunctivitis

Allergic conjunctivitis occurs when an allergic reaction causes conjunctivitis, an inflammation of the thin layer of tissue that lines the outside of the white surface of the eye and the inner surface of the eyelids. It may affect one or both eyes. The signs and symptoms may include eye redness, excessive watering, itchy, burning eyes, discharge, blurred vision and increased sensitivity to light.

It is estimated that more than 75 million people suffer from allergic conjunctivitis in the U.S. and the estimated prevalence of allergic conjunctivitis may be between 15% and 40%. The annual U.S. market for prescription treatment of allergic conjunctivitis totals approximately $257 million in 2021 according to IQVIA Health Analytics, which does not include substantial sales of over-the--counter eye drops. Branded prescription products represent around 30% market share by value. There was an impairment (€12.7 million) to the value of ZERVIATE in the U.S. in 2021 taking into consideration changes in the U.S. market for topical anti-allergics and consequently the net book value of ZERVIATE corresponds mainly to the value of the asset allocated to the Chinese territory, for which the rights were granted to the partner Ocumension.

Non-core partnered program

Naproxcinod

Naproxcinod is a Cyclooxygenase-Inhibiting Nitric–Oxide Donating, or CINOD, anti-inflammatory product candidate, which is partnered with Fera Pharmaceuticals in the U.S. Fera have been reviewing opportunities for the development of naproxcinod in a number of indications and have conducted nonclinical development work on naproxcinod in models of both COVID-19 infections and sickle cell disease. Efforts will continue focusing on sickle cell disease and other undisclosed therapeutic indications in which the properties of naproxcinod may be beneficial. In February 2022, Fera received an Orphan Drug Designation (ODD) from the FDA for the use of naproxcinod for the treatment of sickle-cell disease.

We had previously completed a broad clinical program for naproxcinod in osteoarthritis, including three Phase 3 trials with over 2,700 patients. We submitted an NDA for naproxcinod for osteoarthritis in 2009 and received a Complete Response Letter in 2010 in which the FDA requested substantial additional long-term safety data on the product. We do not plan to further develop naproxcinod- for osteoarthritis.

1.2.2. Commercial, Industrial, and financial contracts and Intellectual Property

1.2.2.1. Our Collaboration Agreements

Bausch + Lomb

In March 2010, we signed an exclusive worldwide licensing agreement with Bausch + Lomb, a leading global eye health company, granting Bausch + Lomb exclusive worldwide rights to develop and market latanoprostene bunod. Latanoprostene bunod is commercialized by Bausch + Lomb under the brand name VYZULTA which is commercialized in more than 15 countries, including the U.S., and is also approved in a number of other countries Bausch + Lomb is responsible for funding development and marketing activities, and we jointly manage the collaboration with them through a joint executive committee. The agreement also grants Bausch + Lomb the exclusive worldwide rights to develop and market other products containing latanoprostene bunod, such as fixed dose- combinations, for the reduction of IOP and/or the treatment of glaucoma.

Under the terms of the agreement signed in 2010, Bausch + Lomb made an initial license payment of $10 million to us upon execution of the agreement. Bausch + Lomb made an additional $10 million milestone payment to us in April 2012 following the decision to pursue further development of latanoprostene bunod after the Phase 2 clinical trial completion in late 2011.

As a result of the FDA's approval of VYZULTA in November 2017, we received a $17.5 million milestone payment from Bausch + Lomb and we made a $15 million milestone payment to Pfizer under the 2009 agreement whereby we regained the rights to latanoprostene bunod. In March 2018, we and Bausch + Lomb amended the agreement signed in 2010. The amendment provides that, from January 1, 2019, the royalties due to us according to the original agreement will increase by 1% over the original royalty on net sales above $300 million per year. Royalties will now be 10% to 16% over four tiers, reaching the maximum tier if and when global net sales exceed $500 million annually. Considering our royalty payments to Pfizer, the net royalties to us will be 6% to 12%, compared to 6% to 11% originally. These royalties could continue to 2030 in the U.S., subject to a Patent Term Extension, and beyond 2030 in other countries, depending on the date of launch of VYZULTA. In addition, the potential milestones payable to us by Bausch + Lomb have been increased by $20 million, added to and split among three existing milestones at increasing annual net sales levels. The first additional amount payable will be added to the milestone on achievement of $300 million annual net sales and the last additional amount payable will be added to the milestone on achievement of $700 million annual net sales. The total potential milestones due to us have therefore been increased from $145 million to $165 million. We are eligible to receive a $5 million net ($20 million before deductions to Pfizer) milestone on VYZULTA net sales reaching $100 million and are receiving tiered net royalties from Bausch + Lomb of 6% to 12%, after deduction of payments due to Pfizer under the 2009 agreement.

Pursuant to our agreement with Bausch + Lomb, we had an option to co-promote latanoprostene bunod products in the U.S. In August 2014, we informed Bausch + Lomb of our decision to exercise the option. However, we have since agreed with Bausch + Lomb that we will not co-promote latanoprostene bunod in the U.S.

Additionally, Bausch + Lomb had the option, pursuant to our agreement, to develop additional NO-donating compounds for the reduction of IOP and/or the treatment of glaucoma, including other NO-donating prostaglandin F2-alpha analogs from our research. During the third quarter of 2013, Bausch + Lomb decided to forego this option.

Our licensing agreement with Bausch + Lomb will remain in effect until all royalty payment obligations from Bausch + Lomb expire or unless terminated earlier by either us or Bausch + Lomb

pursuant to the early termination provision in the agreement. The duration of royalty obligations under the agreement exists on a country-by-country and licensed product-by-licensed product basis, and commences on the date of first commercial sale for the particular country and the particular licensed product and terminates on the latest of (i) the date on which there exists no subsisting claim of an unexpired patent or collaborative patent covering latanoprostene bunod or a licensed product; (ii) the date of expiration of any period of marketing exclusivity, data protection or data exclusivity applicable to such licensed product in the relevant country; and (iii) ten years after the date of first commercial sale date. If there has been no launch date for a licensed product prior to the expiration of (i-) and (ii), the royalty obligation terminates on the later expiring of (i-) and (ii).

We may terminate the agreement on a country-by-country basis if Bausch + Lomb fails to use commercially reasonable efforts to develop and commercialize the licensed products. We may also terminate the agreement in its entirety in the event that Bausch + Lomb challenges or causes a third party to challenge the validity or ownership of any of our licensed patents or fails or becomes unable to meet its payment obligations under the agreement. Bausch + Lomb may terminate this agreement without cause upon 90 days' notice. In the event of termination, except in the event of expiration of the payment obligations of Bausch + Lomb, licenses granted by us to Bausch + Lomb will terminate and any sublicenses granted by Bausch + Lomb will either be assigned to us or terminated.

Eyevance Pharmaceuticals

In September 2017, we entered into an exclusive license agreement with Eyevance, a wholly owned subsidiary of Santen Pharmaceutical Co., Ltd, for the commercialization of ZERVIATE in the U.S.

Under the agreement, Eyevance made a onetime nonrefundable upfront payment to us of $6.0 million in 2017 and a milestone payment $3.0 million in July 2019 resulting from the achievement by us of certain manufacturing and regulatory objectives. We are eligible to receive up to an additional $37.5 million in future milestones payable on -Eyevance achieving predefined sales targets, with $30 million of these milestones being triggered by annual sales targets of $100 million and above. In addition, we will also receive tiered royalties of 8% to 15% based on future net sales of ZERVIATE. We also are committed to paying -Eyevance- $469,000 related to manufacturing costs that resulted from a delay in the completion of certain manufacturing activities. This amount will be directly deducted from royalty payments.

Eyevance has the exclusive right to commercialize ZERVIATE in the U.S. where it has been marketed since March 2020. In February 2021, Eyevance entered into a partnership with Hikma Pharmaceuticals for promoting ZERVIATE to U.S. healthcare professionals working outside the eyecare specialty, with all sales continuing to be booked by Eyevance, on which Nicox will receive royalties.

The license agreement with Eyevance will remain in force until the later of the fifteenth anniversary of the commercial launch of ZERVIATE or until the expiry of the last licensed patent in the U.S. Eyevance has the right to renew the agreement for two additional five-year periods with three months' advance notice. Additionally, with 90 days' prior written notice, Eyevance can terminate the agreement for convenience and either party can terminate the agreement upon a material breach by the other party following a 90-day cure period. In the event of expiry or termination of the agreement, Eyevance and certain related parties may complete and sell any work-in--process and product inventory that exists as of the date of termination. Upon termination, all rights granted to Eyevance- terminate.

Fera Pharmaceuticals

In November 2015, we entered into an exclusive license agreement with Fera, granting Fera exclusive rights to develop and commercialize naproxcinod in the U.S. The agreement was amended in September 2018, in December 2020 and May 2022.

Under the terms of the amended agreement, we may be eligible to receive up to $40 million in a single, onetime only, sales-based milestones if annual sales of naproxcinod reach $1 billion (in any indication), plus 7% royalties based on net sales of naproxcinod in the U.S. In the event of development of naproxcinod for COVID-19, the rights granted to Fera could, under certain conditions, also include the European Union and the United Kingdom. Fera will be responsible for, and will fully finance, all clinical development, manufacturing, and commercialization activities. The agreement covers all indications excluding ophthalmology- related conditions and Duchenne Muscular Dystrophy, or DMD, and we will retain all rights for naproxcinod outside of the U.S. Fera is eligible to receive an undisclosed royalty should we sell or license rights to sell naproxcinod or related products in any ex-U.S. territory to a third party if the third party uses any Fera intellectual property, regardless of the therapeutic indication and territory. A joint steering committee will be put in place with representation from both companies to ensure that development of naproxcinod- proceeds in accordance with the agreement.

The contract remains in force until the later of the tenth anniversary of the commercial launch or the expiration of the last patent included in the agreement. Upon termination of the agreement due to expiration of the term or our material breach, the licenses become fully paid and irrevocable and Fera will have all rights to the product in the U.S. In the case where Fera, despite having used commercially reasonable efforts, has not submitted an NDA for the product before December 31, 2027, Fera must present a plan for such submission, otherwise we may terminate the agreement. Fera may terminate the agreement at any time by giving one month's notice. In such case (or in the case of material breach by Fera), all the rights concerning regulatory authorizations, intellectual property rights concerning the product and all data (including clinical, preclinical, regulatory, formulation and commercial data) shall be assigned or licensed (if assignment is not possible) to us.

ITROM Pharmaceutical Group

In August 2020 we entered into an exclusive license agreement with ITROM Pharmaceutical Group for the registration and commercialization of ZERVIATE for the treatment of ocular itching associated with allergic conjunctivitis in Gulf and Arab markets including the Kingdom of Saudi Arabia, the United Arab Emirates and Qatar. ITROM is a regional, Dubai-based, internationally recognized pharmaceutical marketing and distribution group of companies specializing in the introduction and representation of breakthrough ophthalmology products since 1999.

Under the terms of the agreement ITROM is granted exclusive rights to develop and commercialize ZERVIATE in Bahrain, Egypt, Iraq, Jordan, Kuwait, Libya, Oman, Qatar, the Kingdom of Saudi Arabia, the United Arab Emirates and Yemen. Nicox is eligible to receive 15% royalties on net sales of ZERVIATE in certain key countries, and 10% in other countries. Nicox will also receive a license fee on signature and may receive a future milestone payment upon product launch. ITROM will be responsible, at its own cost, for development and commercialization of ZERVIATE in the countries of the agreement. ZERVIATE is expected to require only the existing approved U.S. New Drug Application (NDA) package to support approval.

Laboratorios Grin

In May 2021 we entered into an exclusive license agreement with Laboratorios Grin, for the registration and commercialization of ZERVIATE™ (cetirizine ophthalmic solution), 0.24% for the treatment of ocular itching associated with allergic conjunctivitis in Mexico. Grin, a wholly owned subsidiary of Lupin Limited, is a Mexican specialty pharmaceutical company engaged in the development, manufacturing and commercialization of branded ophthalmic products.

Grin is granted rights to develop and commercialize cetirizine ophthalmic solution, 0.24% in Mexico. Nicox will receive an undisclosed license fee and potential milestone payments linked to regulatory approval and sales and is eligible to receive double digit royalties on net sales of ZERVIATE. Grin will be responsible, at its own cost, for the development, manufacturing, and the commercialization of ZERVIATE in Mexico.

Ocumension Therapeutics

In December 2018 we entered into an exclusive license agreement with Ocumension Therapeutics for the development and commercialization of Nicox's product candidate, NCX 470, targeting patients with glaucoma or ocular hypertension for a territory comprising mainland China, Hong Kong, Macau, and Taiwan, or the Chinese market. NCX 470 is currently in the Phase 3 trial, Denali, jointly conducted and equally financed by Nicox and Ocumension. The first Phase 3 trial, Mont Blanc, has been completed and results announced in October 2022. Mont Blanc and Denali have been designed to fulfill the regulatory requirements for Phase 3 safety and efficacy trials to support NDA submissions of NCX 470 in the U.S. and China and will also provide data for countries accepting the same clinical data package for approval. All development activities are overseen by a Joint Governance Committee comprising representatives of both companies, with Ocumension responsible for undertaking all the activities at its own cost. Under the agreement signed in 2018, Ocumension received exclusive rights to develop and commercialize NCX 470, at its own cost, in the agreed territory. Under the terms of the agreement, we received a onetime upfront payment of €3 million from Ocumension and Nicox was eligible to receive a further €2.5 million when we initiate a Phase 3 clinical trial with NCX 470 outside the territory of this agreement. Nicox was also eligible to receive up to an additional €14.5 million in milestones associated with Ocumension's progress with NCX 470, up to and including regulatory approval, and up to €16.25 million split over three separate sales milestones associated with potential sales in the territory of up to € 200 million, as well as tiered royalties from 6% to 12% on sales.

The agreement was amended in March 2020 and under the terms of this new amendment, Ocumension paid Nicox €15 million (in replacement of the totality of the milestones in the original agreement), gained additional exclusive rights to NCX 470 for Korea and Southeast Asia and agreed to pay 50% of the costs of the second glaucoma Phase 3 clinical trial Denali of NCX 470. No future NCX 470 milestones will be due from Ocumension to Nicox. In the case that the Denali trial would not take place, partial or limited refunds of this payment may be due. The tiered royalties of 6% to 12% of the original agreement remain unchanged and will apply to sales in the original and the additional territories.

In March 2019 we entered into an exclusive license agreement with Ocumension for the development and commercialization of Nicox's product ZERVIATE for the treatment of allergic conjunctivitis for the Chinese market. Ocumension received exclusive rights to develop and commercialize ZERVIATE, at its own cost, in the agreed territory. The agreement was amended in March 2020 granting Ocumension additional exclusive rights of ZERVIATE in the majority of the Southeast Asian region. Under a new amendment in July 2021, Ocumension paid Nicox $2 million in full advance payment of the future development and regulatory milestones for ZERVIATE. Nicox remains eligible to receive the same sales milestones of up US$17,2 million together with tiered

royalties of between 5% and 9% on net sales of ZERVIATE by Ocumension. Potential annual net sales are forecasted by Ocumension over $100 million within 7 years in China. Other terms of the original agreement remain unchanged. All development activities will be overseen by a Joint Governance Committee comprising representatives of both companies, with Ocumension responsible for undertaking all the activities at its own cost. In February 2022 Ocumension completed a confirmatory Phase 3 clinical trial for ZERVIATE in China and submitted New Drug Application for the Chinese market in April 2023. The NDA has been included in the priority review and approval process of National Medical Products Administration of the People's Republic of China ("NMPA"). This will accelerate the approval process and launch of ZERVIATE expected in China in 2024.

In June 2019, we entered into an exclusive license agreement with Ocumension for the development and commercialization of Nicox's product candidate, NCX 4251, for blepharitis in the Chinese market. Ocumension is responsible, at its own cost, for all development activities necessary for the approval of NCX 4251 in the territory, overseen by a Joint Governance Committee comprising representatives of both companies. Ocumension received exclusive rights for the agreed territory to develop and commercialize NCX 4251 in blepharitis. As provided for in the terms of the agreement, Nicox and Ocumension subsequently agreed to change the target indication for dry eye without any change in financial or other contractual terms. Under the terms of the agreement, Nicox received an upfront payment of US$ 2.3 million and may potentially receive development and sales milestones of up to US$ 11.3 million together with tiered royalties of between 5% and 10% on sales of NCX 4251.

Pfizer

In August 2009, we signed an agreement with Pfizer terminating our previous collaboration agreements dated August 2004 and March 2006. Under the terms of the 2009 agreement, we recovered all the development and marketing rights for latanoprostene bunod, and in particular the right to sublicense, as well as all the data and development information. This compound is currently outlicensed to Bausch + Lomb (see above). Moreover, we also have access to certain information regarding development of XALATAN (latanoprost ophthalmic solution) 0.005% belonging to Pfizer, in particular the regulatory files for XALATAN (latanoprost ophthalmic solution) 0.005%. In return, we are obligated to pay Pfizer two milestone payments of $15 million each linked to approval of VYZULTA in the U.S. (or a lower amount if approved only in Europe or Japan) and $15 million linked to reaching predefined sales levels. The first milestone payment was made in December 2017. Pfizer is also entitled to receive royalties on potential future sales. Pfizer's royalties are in the low single digit percentages for sales in the U.S. and sales made directly by us outside the U.S. For sales made by our licensees outside the U.S., Pfizer's royalty is the greater of our royalty rate for sales outside the U.S. or a low double--digit- percentage of the income that we receive from such licensee. We also recovered the rights to a certain number of new NO donors at the research stage for the potential treatment of diabetic retinopathy and glaucoma.

Samil Pharmaceutical

In December 2019 we entered into an exclusive license agreement with Samil Pharmaceutical Co., Ltd, or Samil, for the development and commercialization of ZERVIATE (cetirizine ophthalmic solution), 0.24% for the treatment of ocular itching associated with allergic conjunctivitis in South Korea. Samil received exclusive rights to develop and commercialize ZERVIATE in South Korea and the agreement was expanded in February 2022 to include Vietnam. Samil is considered as one of the leading Korean companies specialized in the field of ophthalmic medicines including the research and development of drugs in the field of ophthalmology.

Nicox is eligible to receive 10% royalties on net sales on ZERVIATE in South Korea and a milestone payment of 5% of net sales for each calendar year in which net sales exceed approximately US $900,000 (at current exchange rates). Nicox will also receive a license fee, and may receive approval and launch milestone payments which, together with the license fee, may total almost US $250,000. Samil will be responsible, at its cost, for development and commercialization of ZERVIATE in South Korea and in Vietnam. ZERVIATE is expected to require only manufacturing transfer and associated pharmaceutical development to support approval in South Korea, in addition to the existing approved U.S. NDA package.

1.2.2.2. Other Partnerships

We have other partnerships that are not active at this time. For instance, under our collaboration with Portola Pharmaceuticals, Inc., we have exclusive rights to jointly develop certain of their preclinical small molecules for topical ophthalmic indications, but no compound has been selected for development under this agreement. Under our collaboration with Merck, Merck can elect to develop certain of our NO-donating- compounds in the cardiovascular field. We do not expect these partnerships to impact on our future financial status at this time.

1.2.2.3. Manufacturing and Supply

We do not have any in-house manufacturing facilities or logistics platforms. Therefore, we need to secure agreements with third parties for the manufacturing and supply of our product candidates under development. These third parties either manufacture and assemble in-house or outsource one or more processes to other external service providers.

Our business is subject to risks associated with our reliance on third-party suppliers. These risks are discussed more fully in the section of this prospectus titled “Risk Factors.”

1.2.3. Patents

1.2.3.1. Intellectual property protection policy

Intellectual property is of vital importance to the Company's business. Nicox takes all possible measures to protect intellectual property, including by obtaining and maintaining patent protection in different territories (particularly in the U.S.) for its products under development and other inventions important for its business. The Group must also use of trade secrets to protect and ensure the confidentiality of proprietary information to protect those aspects of its business operations that do not lend themselves to patent protection or considered by Nicox as not appropriate for patent protection. The Company must also have recourse to the filing of trademarks, copyrights and contractual obligations to establish and protect its intellectual property rights.

Nicox's activities are dependent on its intellectual property and as such are subject to risks linked to the uncertain protection offered by patents and other intellectual property rights. The position of pharmaceutical companies like Nicox with respect to patents is highly uncertain and involves extremely complex legal, scientific and factual circumstances. In addition, the protections sought in patent applications may be significantly reduced before the patent is issued and its scope may be reinterpreted after it is issued. For that reason, the possibility cannot be excluded that Nicox might not be successful in obtaining or maintaining a patent protection for one of its products under development. The Company cannot anticipate if the patent applications currently pending will result in the issuance of patents in all the targeted territories, or if the claims of the patents issued will offer sufficient protection against the competition. Any patent held by the Company may be challenged, circumvented or invalidated by third parties. The reader is invited to refer to section 3 “risk factors” of the universal registration document that describes the risk factors related to the uncertain protection provided by patents and other intellectual property rights.

The Group has a patent department within its Italian subsidiary Nicox Research Institute Srl. The Group’s patent department regularly uses intellectual property law firms in several countries around the world.

Nicox also relies on trade secret protection for its confidential and proprietary information. Even though the Group takes measures to protect its proprietary information and trade secrets, including through contractual provisions with its employees and consultants, third parties may develop independently information and proprietary techniques substantially equivalent or gain access to its trade secrets or disclose its technology. For those reasons, Nicox might not be able to effectively protect its trade secrets. The company's policy requires staff, consultants, external scientific staff and other consultants to sign confidentiality agreements at the start of their employment or relations as consultants with Nicox. The agreements thus concluded with employees also provide that all inventions designed by an employee in the course of his or her term of employment within the Company or based on the use of confidential information of the Company remain the exclusive property of Nicox.

1.2.3.2. Nature and coverage of patent families owned by the Company

As of December 31, 2022, our patent portfolio included 432 issued patents and 122 pending patent applications and 4 patent applications under the Patent Cooperation Treaty (PCT). In the U.S., our patent portfolio includes 46 issued patents and 12 pending patent applications. We also have 19 patents granted by the European Patent Office, which have been validated in the principal European countries, and 9 pending European patent applications.

Latanoprostene bunod (the active ingredient of VYZULTA) is protected in the U.S. by four granted patents which expire in 2025. A patent term extension (PTE) application was filed in December 2017. In March 2021 the U.S. Patent and Trademark Office (USPTO) issued a communication confirming that the patent covering VYZULTA is eligible for PTE. The USPTO will take about two years to

make the final determination and issue of a PTE certificate. The PTE could provide additional protection until 2030.

On May 17, 2022, Gland Pharma Limited submitted a Notice of Paragraph IV certification concerning the patent protection of Vyzulta® referenced in the FDA's Orange Book.

In Europe, a patent covering latanoprostene bunod (the active ingredient of VYZULTA) was issued in February 2016 and validated in 36 countries of the European Patent Convention (EPC) and will provide protection until 2024. An application could be made for a Supplementary Protection Certificate (SPC) to extend the term of the patent to a maximum of 5 years.

On November 23, 2016, Teva Pharmaceutical Industries Ltd. filed a notice of opposition against the grant of the European patent covering latanoprostene bunod. On July 13, 2018, the Opposition Division rejected the opposition and decided to maintain the patent as granted. On September 12, 2018, Teva Pharmaceutical Industries Ltd. filed an appeal against the decision of the Opposition Division. On June 20, 2022, TEVA Pharmaceutical Industries withdrew the Appeal and on July 7, 2022, the Board of Appeal closed the appeal proceedings; the decision of the Opposition became final, and the patent is maintained as granted.

In Japan, latanoprostene bunod (the active ingredient of VYZULTA) is protected by a patent which expires in 2024.

ZERVIATE is protected in the U.S. by four patents expiring in 2030 and 2032 listed in the FDA's Approved Drugs Products with Therapeutic Equivalence Evaluation (commonly known as the Orange Book). On January 5, 2022, The European Patent Office (EPO) publishes the grant of the European patent covering Zerviate. This patent will offer protection until 2030.

In Japan, ZERVIATE is covered by three patents expiring in March 2030.

NCX 4251 is protected in the U.S. and in Europe by patents which expire in 2033.

In July 2020, Nicox filed a PCT application and national patent applications in the U.S., Europe (EPC), China, Japan, Taiwan and Argentina covering the process for the preparation of the NCX 4251 formulation under development and the NCX 4251 formulation as product. The European, Japanese and Chinese patents were granted, these patents provide protection until 2040 as well as the other members of this patent family which, if granted, will provide worldwide patent coverage until 2040.

NCX 470 is covered by a patents family which includes the granted patent US 8,101,658 expiring in 2029 and the European patent EP 2 274 279 which was validated in France, Germany, Italy, Spain and the United Kingdom. The product patent family also includes patents granted in Canada, Japan, China, Hong Kong, Argentina and India which are in force until 2029. Patent US 8,101,658 is eligible for a patent term extension which, if granted, may extend the expiration date for a period of up to five years.,

In July 2019, Nicox filed a PCT application and national patent applications in USA, Europe (EPC), China, Japan, Taiwan, and Argentina covering the NCX 470 formulation under development. The U.S., the European, the Japanese and the Chinese patents were granted extending patent coverage of the NCX 470 formulation to 2039.

In February 2018 Nicox filed an European patent application and, in February 2019, a correspondent PCT application covering an industrial process of synthesis of NCX 470. In Europe the patent was granted on September 30, 2020, and it was validated in 17 member States of the European Patent Convention (EPC); this patent provides protection for the process and the product prepared by the process until 2038. The US national patent application deriving from the PCT application was granted in April 2021, the US patent as well as the other national applications, if granted, will provide

worldwide patent coverage for NCX 470 until 2039. In 2020 and 2022, Nicox filed three additional patent applications covering improved processes for the synthesis of NCX 470. The patent families deriving from these patent applications, if granted, will provide additional protection for NCX 470 until 2042.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a nonprovisional patent application.

In the U.S., the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent.

The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions. In the future, if our products receive FDA approval or other regulatory authorities, we expect to apply for patent term extensions on patents covering one or more of those products. However, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted and, if granted, the length of such extensions.

The following tables summarize the status of our current patent portfolio for Nicox products and key product candidates as of December 31, 2022. For each family of patents, a table shows the different members of the family in force, by country, with the maximum possible expiration date subject to regular payment of maintenance fees and the absence of questioning of the validity of the patent concerned

VYZULTA (latanoprostene bunod)

Patent title: PROSTAGLANDIN DERIVATIVES

This patent family covers nitrooxy-derivatives of prostaglandin F2α analogues having improved pharmacological activity and enhanced tolerability and their use for the treatment of glaucoma and ocular hypertension.

Latanoprostene bunod, its use for the treatment of glaucoma and ocular hypertension and its pharmaceutical formulations are specifically disclosed and claimed.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date *
Granted	Europe#	EP 1 704 141	27-Dec-2004	24-Feb-2016	27-Dec-2024
	Europe§	EP 3 002 277	27-Dec-2004	16-Nov-2019	27-Dec-2024
	U.S.	US 7,273,946^	05-Jan-2005	25-Sep-2007	03-Oct-2025
	U.S.	US 7,629,345^	05-Jan-2005	08-Dec-2009	05-Jan-2025
	U.S.	US 7,910,767	05-Jan-2005	22-Mar-2011	05-Jan-2025
	U.S.	US 8,058,467^	05-Jan-2005	15-Nov-2011	05-Jan-2025
	U.S.	US 7,449,469	05-Jan-2005	11-Nov-2008	05-Jan-2025
	Japan	JP 3 984 283	27-Dec-2004	13-July-2007	27-Dec-2024
	China	CN 100469765	27-Dec-2004	18-Mar-2009	27-Dec-2024
	37 other countries		Dec-2004/Jan-2005	Aug-2006/May-2018	Dec-2024 / 5-Jan-2025
Pending	6 countries		27-Dec-2004	-	27-Dec-2024

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.
(#) EP 1 704 141 was validated in 37 member States and Extension States of the European Patent Convention (EPC). On November 23, 2016, TEVA Pharmaceutical Industries Ltd, or TEVA, filed a Notice of Opposition at the EPO. On July 13, 2018, the Opposition Division decided to reject the Opposition and to maintain the patent as granted. A notice of appeal against the decision of the Opposition Division was filed by TEVA Pharmaceutical Industries Ltd on September 12, 2018. On March 2019, Nicox filed a reply to the grounds of appeal. On June 20, 2022, TEVA withdrew the Appeal. On July 7, 2022 the Board of Appeal closed the appeal proceedings. The decision of the Opposition Division became final and the patent is maintained as granted.
(§) EP 3 002 277 was validated in FR, DE, IT, GB, ES and IE
(^) U.S. 7,273,946, U.S. 7;629,345and U.S. 8,058,467 are listed in the FDA's Orange Book for VYZULTA
On May 17, 2022, Gland Pharma Limited submitted a Notice of Paragraph IV certification concerning the patent protection of Vyzulta® referenced in the FDA's Orange Book
In December 2017, Nicox filed requests for PTE for U.S. 7,273,946, U.S. 8,058,467 and U.S.7,629,345 at the USPTO.
In April 2021 the U.S. Patent and Trademark Office (USPTO) issued a communication confirming that the patents covering VYZULTA are eligible for PTE.

NCX 470 (NO-donating bimatoprost)

Patent title: NITRIC OXIDE DONATING PROSTAMIDES

This patent family covers nitrooxyderivatives of bimatoprost and their use for treating glaucoma and ocular hypertension.

NCX 470 is specifically disclosed and claimed.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Application n°	Filing Date	Issue Date	Expiry date*
Granted	Europe#	EP 2 274 279	11-May-2009	31-July-2013	11-May-2029
	U.S.	US 8,101,658	11-May-2009	24-Jan-2012	11-May-2029
	Japan	JP 5 401 540	11-May-2009	01-Nov-2013	11-May-2029
	China§	CN 102099330	11-May-2009	30-Apr-2014	11-May-2029
	Canada	CA 2,723,704	11-May-2009	22-Aug-2017	11-May-2029
	India	IN 307590	11-May-2009	19-Feb-2019	11-May-2029
	Argentina	AR 076731	11-May-2009	31-Oct-2016	11-May-2029

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.
(#) EP 2 274 279 was validated in FR, DE, IT, GB and ES.
(§) Chinese patent was extended into Hong Kong (HK 1160835)

NCX 470 eye drop formulation

Patent title: OPHTHALMIC COMPOSITIONS CONTAINING A NITRIC OXIDE RELEASING PROSTAMIDE

This patent family covers aqueous ophthalmic compositions in the form of solution containing NCX470 and macrogol 15 hydroxystearate as the only solubilizing agent, and a method for their preparation.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Granted	Europe[#]	EP 3 593 788	10-July-2019	28-Oct-2020	10-July-2039
	U.S.	US 10,688,073	10-July-2019	23-June-2020	10-July-2039
	U.S.	US 11,020,368	11-Mar-2020	01-June-2021	10-July-2030
	China[§]	CN 110237031	10-July-2019	11-Feb-2022	10-July-2039
	China[§]	CN 111249228	4-Mar-2020	03-May-2022	10-July-2039
	Japan	JP 7080268	4-Mar-2020	26-May-2022	10-July-2039
	Japan	JP 6672512	10-July-2019	02-Mar-2022	10-July-2039
	Brunei Darussalam	BN/N/0001/2021	10-July-2019	29-Dec-2021	10-July-2039
Pending	Europe	EP 3 718 535	29-Apr-2020	-	10-July-2039
	U.S.	US 2021-0128458	11-Jan-2021	-	10-July-2039
	U.S.	US 2021-0220316	29-Mar-2021	-	10-July-2039
	Japan	JP 2022-084562	24-May-2022	-	10-July-2039
	17 other countries	-	10-July-2019	-	10-July-2039

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.
(#) EP 3 583 788 was validated in 38 States of the European Patent Convention (EPC) and in Bosnia-Herzegovina, Montenegro, Moldova, Morocco, Tunisia and Hong Kong and registered in Cambodia.
(§) Chinese patents were extended into Hong Kong and Macao (J/005948, J/006238)

NCX 470 preparation process

Patent title: PROCESS FOR THE PREPARATION OF A NITRIC OXIDE DONATING PROSTAGLANDIN ANALOGUE

This patent family covers a process for large scale preparation of Hexanoic acid, 6-(nitrooxy)-, (1S,2E)-3-[(1R,2R,3S,5R)-2-[(2Z)-7-(ethylamino)-7-oxo-2-hepten-1-yl]-3,5-dihydroxycyclopentyl]-1-(2-phenylethyl)-2-propen-1-yl ester (NCX470).

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Granted	Europe[#]	EP 3 530 649	21-Feb-2018	30-Sept-2020	21-Feb-2038
	Europe[§]	EP 3 757 089	10-July-2020	11-May-2022	21-Feb-2028
	U.S.	US 10,988,438	12-Feb-2019	27-apr-2021	12-Feb-2039
Pending	China	CN 111757868	12-Feb-2019	-	12-Feb-2039
	Japan	JP 2021-514371	12-Feb-2019	-	12-Feb-2039
	14 other countries	-	Feb-2019	-	12-Feb-2039

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.
(#) EP 3 530 649 was validated in 17 States of the European Patent Convention (EPC).
(§) EP 3757 089 was validated in FR, DE, IT, GB, ES and IE

NCX 470 preparation process

Patent title: PROCESS FOR THE PREPARATION OF A NITRIC OXIDE DONATING PROSTAGLANDIN ANALOGUE

This patent family covers an improved preparation process of Hexanoic acid, 6-(nitrooxy)-, (1S,2E)-3-[(1R,2R,3S,5R)-2-[(2Z)-7-(ethylamino)-7-oxo-2-hepten-1-yl]-3,5-dihydroxycyclopentyl]-1-(2-phenylethyl)-2-propen-1-yl ester (NCX470).

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Pending	Europe	EP 3 772 511	05-Aug-2019	-	05-Aug-2039
	U.S.	US 2022/274924	03-Aug-2020	-	003-Aug-2040
	China	CN 114174261	03-Aug-2020	-	03-Aug-2040
	4 other countries	-	03-Aug-2020	-	03-Aug-2040

(*) Expired date given prior to any potential extension in accordance with the local patent regulations.

NCX 470 preparation process

Patent title: PROCESS FOR THE PREPARATION OF A NITRIC OXIDE DONATING PROSTAGLANDIN ANALOGUE

This patent family covers a process for the preparation of Hexanoic acid, 6-(nitrooxy)-, (1S,2E)-3-[(1R,2R,3S,5R)-2-[(2Z)-7-(ethylamino)-7-oxo-2-hepten-1-yl]-3,5-dihydroxycyclopentyl]-1-(2-phenylethyl)-2-propen-1-yl ester (NCX470) having a high chemical purity. The invention also describes the preparation of highly pure 6-(nitrooxy)hexanoic acid that is a key intermediate of the synthesis.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Active	PCT§	WO 2022/167070	3-Feb-2021	-	-
Pending	2 countries	-	28-Jan-2022	-	28-Jan-2042

(*) Expired date given prior to any potential extension in accordance with the local patent regulations.
(§) PCT application WO 2022/167070 will enter the national/ regional phases in August 2023

ZERVIATE (cetirizine)

Patent title: OPHTHALMIC FORMULATIONS OF CETIRIZINE AND METHOD OF USE

This patent family covers topical ophthalmic formulations comprising cetirizine and its salts wherein cetirizine is present in an amount of 0.1% to 0.25% (w/v), and method for alleviating signs and symptoms of allergic conjunctivitis by topical administration of the ophthalmic formulations.
ZERVIATE, 0.24% cetirizine hydrochloride formulation and its use in the treatment of ocular itching associated with allergic conjunctivitis are specifically claimed.

Patent owner: Nicox Ophthalmics Inc.

Patent status	Territory	Patent n°/ Application n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 9,254,286^	15-Mar-2010	09-Feb-2016	09-July-2032
	U.S.	US 8,829,005^	21-May-2013	09-Sep-2014	15-Mar-2030
	U.S.	US 9,750,684^	29-Dec-2015	05-Sept-2017	15-Mar-2030
	U.S.	US 9,993,471^	10-Mar-2017	12-June-2018	15-Mar-2030
	U.S.	US 8,569,273	22-Sept-2010	29-Oct-2013t	15-Mar-2030
	U.S.	US 10,675,279	06-Jun-2018	09-Jun-2020	15 Mar 2030
	U.S.	US 10,987,352	03-Apr-2020	27-Apr-2021	15 Mar 2030
	Japan	JP 6033677	15-March-2010	04-Nov-2016	15-Mar-2030
	Japan	JP 6144393	12-Aug-2016	19-May-2017	15-Mar-2030
	Japan	JP 6893573	13-May-2020	03-June-2021	15-Mar-2030
	Japan	JP 7088980	13-May-2020	13-June-2022	15-Mar-2030
	Japan	JP 6449202	12-Aug-2016	14-Dec-2018	15-Mar-2030
	Europe[#]	EP 2 408 453	15-Mar-2010	05-Jan-2022	15-Mar-2030
	Canada	CA 2,755,679	15-Mar-2010	12-Sept-2017	15-Mar-2030
Pending	U.S.	US2020/0405711	11-Sept-2020	-	15-Mar-2030
	U.S.	US 2021/0290617	27-May-2021	-	15-Mar-2030
	Europe	EP 3 943 069	16-Jan-2021	-	15-Mar-2030
	Japan	JP 2021138760	15-June-2021		15-Mar-2030

(*) Expired date given prior to any potential extension in accordance with the local patent regulations.
(^) U.S. 9,254,286, U.S. 8,829,005, U.S. 9,750,684 and U.S. 9,993,471 are listed in the FDA's Orange Book for ZERVIATE
(#) EP 2 408 453 was validated in FR, DE, IT, ES, GB, PT and TR

NCX 4251 (Fluticasone propionate nanocrystals Form A)

Patent title: PREPARATION OF HYDROPHOBIC THERAPEUTIC AGENTS, METHOD OF MANUFACTURE AND USE THEREOF

This patent family covers nanocrystals of fluticasone propionate (Form A) wherein the nanocrystals have the c-axis crystallographic direction substantially normal to the surfaces that define the thickness of the nanocrystals and an average particle size of 100 nm to 1000 nm.

This patent family also covers fluticasone propionate (Form A) nanocrystals suspensions, methods for treating or alleviating symptoms of blepharitis, postoperative ocular inflammation, dry eye or eye allergy and the sono-crystallization- process for preparing the fluticasone propionate nanocrystals Form A.

Patent owner: Nicox Ophthalmics Inc.

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 8,765,725	07-Jan-2013	01-July-2014	07-Jan-2033
	U.S.	US 10,174,071	26-July-2018	08-Jan-2019	06-May-2033
	U.S.	US 10,954,263	29-Nov-2018	23-Mar-2021	06-May-2033
	Japan	JP 6285419	06-May-2013	09-Feb-2018	06-May-2033
	Japan	JP 6564891	01-Feb-2018	02-Aug-2019	06-May-2033
	Japan	JP 6752940	17-June-2019	21-Aug-2020	06-May-2033
	Japan	JP 6972255	19-Aug-2020	05-Nov-2021	06-May-2033
	Europe^	EP 2 847 207	06-May-2013	27-March-2019	06-May-2033
	Europe#	EP 3 517 541	11-Feb-2019	15-July-2020	06-May-2033
	China§	CN 107880091	23-Nov-2017	18-Dec-2020	06-May-2033
	China§	CN 104350063	06-May-2013	05-Jan-2018	06-May-2033
	Canada	CA 2,872,845	06-May-2013	09-Nov-2021	06-May-2033
	5 other countries	-	06-May-2013	2018-2020	06-May-2033
Pending	Europe	EP 3 741 772	29-May-2020	-	06-May-2033
	U.S.	US 2021/300963	17-Feb-2021	-	06-May-2033
	3 other countries	-	06-May-2013	-	06-May-2033

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(^) EP 2 847 207 was validated in 13 member States of the European Patent Convention (EPC)
(#) EP 3 517 541 was validated in 25 member States of the European Patent Convention (EPC)
(§) Chinese patents were extended into Hong Kong and Macao (HK 1207087, HK 1252481, J/004743)

NCX 4251 (Fluticasone propionate nanocrystals Form A suspensions)

Patent title: PROCESS FOR THE PREPARATION OF STERILE OPHTHALMIC AQUEOUS FLUTICASONE PROPIONATE FORM A NANOCRYSTALS SUSPENSION**S**

This patent family covers the preparation of aqueous suspensions containing nanocrystals of fluticasone propionate (Form A) having an average particle size of 100 nm to 1000 nm.

This patent family also discloses the Fluticasone propionate nanocrystals suspension under development and method for treating blepharitis, posterior blepharitis, Meibomian gland dysfunction or dry eye disease wherein the method comprises topically applying to eyelids, eyelashes or eyelid margin the ophthalmic aqueous nanosuspension.

Patent Owner: Nicox Ophthalmics Inc.

Patent status	Territory	Patent n° / Publication n°	Filing Date	Issue Date	Expiry date*
Granted	Europe[§]	EP 3 769 753	21-July-2020	17-Nov-2021	21-July-2040
	U.S.	US 11,406,596	21-July-2020	09-Aug-2022	21-July-2040
	China[#]	CN 111821261	21-July-2020	26-July-2022	21-July-2040
	Japan	JP 7021301	21-July-2020	07-Feb-2022	21-July-2040
Pending	U.S.	US 2022/241296	21-Jan-2022	-	21-July-2040
	U.S.	US 2022/0323352	27-July-2022	-	21-July-2040
	Japan	JP 2022062172	3-Feb-2022		21-July-2040
	China	CN 115120557	21-July-2020	-	21-July-2040
	17 other countries		21-July-2020	-	21-July-2040

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.
(§) EP 3 769 753 was validated in all the States (38) of the European Patent Convention (EPC) and in Bosnia Herzegovina, Montenegro, Moldova, Morocco and Tunisia and registered in Cambodia,
(#) Chinese patent was extended into Hong Kong and Macao

NCX 4280 (formerly AC-120)

Patent title: METHOD FOR THE TREATMENT AND PREVENTION OF EYELID SWELLING

This patent family covers the use of a composition comprising oxymetazoline and glycerin for treating eyelid swelling.

This patent family also discloses topical pharmaceutical compositions comprising an osmotically active agent and a vasoconstrictor agent. The preferred osmotically active agent is glycerin, and the vasoconstrictor agent is selected from oxymetazoline or naphazoline.

Patent owner: Nicox Ophthalmics Inc.

Patent status	Territory	Patent n° / Publication n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 8,685,439	26-Apr-2007	01-Apr-2014	09-July-2030
Pending	U.S.	US 2021/0177807	07-Dec-2020	-	26-Apr-2027

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

NCX 4240

Patent title: COMPOSITION EFFECTIVE AGAINST VIRAL CONJUNCTIVITIS

The patent family covers a pharmaceutical composition comprising iota carrageenan as the active antiviral ingredient and their use in the prophylactic or therapeutic topical treatment of viral eye infections caused by adenovirus of subtype D or influenza A virus of subtype H7.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date
Granted	U.S.	US 10,220,055	20-Jan-2015	05-Mar-2019	20-Jan-2035
	Canada	CA 2,937,402	20-Jan-2015	12-July-2022	20-Jan-2035
	Japan	JP 6635343	20-Jan-2015	27-Dec-2019	20-Jan-2035
	Mexico	MX 375356	20-Jan-2015	23-Sept-2020	20-Jan-2035

NO-donating prostaglandins

Patent title: NITRIC OXIDE RELEASING PROSTAGLANDIN DERIVATIVES FOR TREATING NORMAL TENSION GLAUCOMA

This patent family covers the use of NCX116 (Vyzulta) in a method to reduce intraocular pressure in a patient having normal tension glaucoma.

Patent owner: Nicox SA and Bausch & Lomb

Patent status	Territory	Patent n° / Publication n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 11,058,691	07-Nov-2017	13-July-2021	21-Mar-2038
	Japan	JP 7055802	07-Nov-2017	08-Apr-2022	07-Nov-2037
Pending	Canada	CA 3,043,000	07-Nov-2017	-	07-Nov-2037
	Brazil	BR1120190093303	07-Nov-2017	-	07-Nov-2037
	Korea	KR 20190104993	07-Nov-2017	-	07-Nov-2037
	Turkey	NA	07-Nov-2017	-	07-Nov-2037

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

NO-donating prostaglandins

Patent title: NITRIC OXIDE DONATING DERIVATIVES OF FLUPROSTENOL

The US granted patent covers 15-nitrooxyderivatives of fluprostenol, the use of said compounds for the treatment of glaucoma and ocular hypertension and pharmaceutical formulation containing 15-nitrooxyderivatives of fluprostenol.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 10,280,138	28-Jan-2016	07-May-2019	28-Jan-2036

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations

NO-donating prostaglandins

Patent title: NITRIC OXIDE DONATING DERIVATIVES OF LATANOPROST FREE ACID

The US granted patent covers 15-nitrooxyderivatives of latanoprost or latanoprost free acid, the use of said compounds for the treatment of glaucoma and ocular hypertension and formulation containing 15-nitrooxyderivatives of latanoprost or latanoprost free acid.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 10,047,047	22-Mar-2016	14-Aug-2018	22-Mar-2036

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations

NO-donating prostaglandins

Patent title: NITRIC OXIDE ENHANCING PROSTAGLANDIN COMPOUNDS, COMPOSITIONS AND METHODS OF USE

The patent family covers nitric oxide enhancing prostaglandin compounds in which the nitric oxide donor group is a heterocyclic molecule, methods for treating ophthalmic disorders comprising administering one nitric oxide enhancing prostaglandin alone or combined with a therapeutic agent.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 8,067,414	19-Mar-2007	29-Nov-2011	31-Jan-2028
	U.S.	US 8,846,674	18-Oct-2011	30-Sept-2014	19-Mar-2027
	Canada	CA 2,647,859	19-Mar-2007	05-Jan-2016	19-Mar-2027

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations

NO-donating PDE5 inhibitors and NCX1728

Patent title: NITRIC OXIDE RELEASING PHOSPHODIESTERASE TYPE 5 INIBITORS

This patent family covers nitric oxide releasing phosphodiesterase type 5 (PDE5) inhibitors. The invention discloses compositions and methods for treating an ocular condition associated with elevated intraocular pressure such as ocular hypertension and glaucoma.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Pending	Europe	EP 3 833 395	31-July-2019	-	31-July-2039
	U.S.	US 2021/322413	31-July-2019	-	31-July-2039
	Japan	JP 2021/533152	31-July-2019	-	31-July-2039
	China	CN 112566670	31-July-2019	-	31-July-2039
	10 other countries		July/Aug-2019	-	July/Aug-2039

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations

NO-donating PDE5 inhibitors and NCX 1728

Patent title: COMPOSITIONS FOR THE TREATMENT OF GLAUCOMA AND OCULAR HYPERTENSION

This patent family covers ophthalmic compositions comprising a NO-PDE5 inhibitor and a prostaglandin analog selected from latanoprost, bimatoprost, travoprost or tafluprost. The invention also relates to the use of these combinations for the treatment of glaucoma, normal tension glaucoma ocular hypertension and eyes diseases or conditions associated with elevated intraocular pressure.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Pending	Europe	EP 4 100 014	03-Feb-2021	-	03-Feb-2041
	U.S.§	NA	03-Feb-2021	-	03-Feb-2041
	Japan§	NA	03-Feb-2021	-	03-Feb-2041
	China	CN 115038449	03-Feb-2021	-	03-Feb-2041
	Canada	CA 3,166,602	03-Feb-2021	-	03-Feb-2041

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) These patent applications are national/regional phases of the PCT application published as WO 2021/156275; the publication numbers are not available yet

Nitric Oxide Donors

Patent title: NITRIC OXIDE DONOR COMPOUNDS

The patent family relates to nitric oxide releasing isohexides (isosorbide, isomannite , isoidite) derivatives and compositions comprising a nitric oxide releasing isohexide derivative and at least one therapeutic agent selected from: NSAIDs, anti-thrombotic drugs, steroidal anti-inflammatory drugs, ACE inhibitors, Angiotensin II receptor antagonist, beta-adrenergic receptor blockers, beta-adrenergic receptor agonists, statins, prostaglandins

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 2 238 143	15-Jan-2009	15-Aug-2012	15-Jan-2029
	U.S.	US 8,003,811	15-Jan-2009	23-Aug-2011	15-Jan-2029
	Japan	JP 5441928	15-Jan-2009	27-Dec-2013	15-Jan-2029
	Canada	CA 2,706,082	15-Jan-2009	3-Oct-2017	15-Jan-2029

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 238 143 was validated in FR, DE, IT, GB and ES

Nitric Oxide Donors

Patent title: QUINONE-BASED NITRIC OXIDE DONATING COMPOUNDS

The patent family covers nitric oxide donor compounds having a quinone-based structure, the processes for their preparation and the use of the compounds for treating pathological conditions in which a deficit of NO plays an important role in their pathogenesis.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 2 707 354	23-Oct-2012	29-Apr-2015	23-Oct-2032
	U.S.	US 9,061,962	23-Oct-2012	23-June-2015	23-Oct-2032
	U.S.	US 9,079,821	22-Jan-2014	14-July-2015	23-Oct-2032
	Japan	JP 6158194	23-Oct-2012	16-June-2017	23-Oct-2032
	China#	CN 103687843	23-Oct-2012	16-Nov-2016	23-Oct-2032
	China#	CN 103739499	13-Jan-2014	7-Sept-2016	23-Oct-2032
	Canada	CA 2,839,390	23-Oct-2012	15-Sept-2015	23-Oct-2032

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 707 354 was validated in FR, DE, IT, GB and ES
(#) Chinese patent was extended into Hong Kong (HK 1196124, HK1197054)

Nitric Oxide Donors

Patent title: QUINONE BASED NITRIC OXIDE DONATING COMPOUNDS FOR OPHTHALMIC USES

The patent family covers quinone-based nitric oxide donor compounds for use in the treatment or prophylaxis of hypertensive glaucoma, normotensive glaucoma and ocular hypertension**.**

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe[§]	EP 2 911 656	10-Oct-2013	02-Dec-2020	10-Oct-2033
	U.S.	US 9,446,015	10-Oct-2013	20-Sept-2016	10-Oct-2033
	Canada	CA 2,888,837	10-Oct-2013	02-Feb-2021	10-Oct-2033
	Japan	JP 6405312	10-Oct-2013	21-Sept-2018	10-Oct-2033
	China[#]	CN 104994845	10-Oct-2013	17-Nov-2017	10-Oct-2033

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 911 656 was validated in FR, DE, IT, GB, IE and ES
(#) Chinese patent was extended into Hong Kong (HK1216505)

Nitric Oxide Donors

Patent title: QUINONE-BASED NITRIC OXIDE DONATING COMPOUNDS FOR OPHTHALMIC USES

The patent family covers nitric oxide donor compounds having a quinone-based scaffold and their use in the treatment or prophylaxis of glaucoma and ocular hypertension

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 2 986 288	14-Apr-2014	12-Apr-2017	14-Apr-2034
	U.S.	US 9,598,349	14-Apr-2014	21-Mar-2017	14-Apr-2034
	Canada	CA 2 909 622	14-Apr-2014	18-May-2021	14-Apr-2034
	Japan	JP 6306148	14-Apr-2014	16-Mar-2018	14-Apr-2034
	China#	CN 105263487	14-Apr-2014	22-Sept-2017	14-Apr-2034

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 986 288 was validated in FR, DE, IT, GB, IE and ES
(#) Chinese patent was extended into Hong Kong (HK1220371)

Nitric Oxide Donors

Patent title: OPHTHALMIC COMPOSITIONS CONTAINING A NITRIC OXIDE DONOR

The patent family covers compositions comprising a 4-nitrooxybutan-1-ol alkyl ester as nitric oxide donor and an ophthalmic drug, the use of said compositions in controlling elevated intraocular pressure associated with glaucoma, ocular hypertension or other diseases or conditions.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 3 021 870	07-July-2014	21-Feb-2018	07-July-2034
	U.S.	US 9,895,335	07-July-2014	28-Feb-2018	07-July-2034
	Canada	CA 2,918,179	07-July-2014	16-Mar-2021	07-July-2034

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 3 021 870 was validated in FR, DE, IT, GB, IE and ES

Nitric Oxide Donors

Patent title: NITRIC OXIDE DONATING CARNOSINE COMPOUNDS

The patent family covers nitric oxide donor carnosine derivatives, processes for their preparation and their use in the treatment or prophylaxis of glaucoma and ocular hypertension.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 2 993 172	4-Sept-2014	19-Apr-2017	04-Sept-2034
	U.S.	US 10,093,696	2-Sept-2015	09-Oct-2018	02-Sept-2035
	Canada	CA 2,959,795	2-Sept-2015	29-Nov-2022	02-Sept-2035
	Japan	JP 6616403	2-Sept-2015	15-Nov-2019	02-Sept-2035
	China#	CN 106795122	2-Sept-2015	27-Sept-2019	02-Sept-2035

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 993 172 was validated in FR, DE, IT, GB, IE and ES
(#) Chinese patent was extended into Hong Kong (HK1237769)

Nitric Oxide Donors

Patent title: COMBINATIONS OF NITRIC OXIDE DONORS AND PROSTAGLANDINS

The patent family covers compositions comprising a nitric oxide releasing isomannide and a prostaglandin F2α analog, the use of the compositions for treating glaucoma and elevated ocular pressure.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 3 220 905	17-Nov-2015	09-Oct-2019	17-Nov-2035
	U.S.	US 10,610,509	17-Nov-2015	07-Apr-2020	17-Nov-2035
	Japan	JP 6820847	17-Nov-2015	07-Jan-2021	17-Nov-2035
	China#	CN 106999452	17-Nov-2015	16-Oct-2020	17-Nov-2035
	Canada	CA 2,968,010	17-Nov-2015	NA	17-Nov-2035

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 3 220 905 was validated in FR, DE, IT, GB, IE and ES
(#) Chinese patent was extended into Hong Kong (HK1241269)

Nitric Oxide Donors

Patent title: NITRIC OXIDE DONOR COMPOUNDS

The patent family covers nitric oxide releasing amino acids derivatives and their use for treating cardiovascular diseases, inflammation, pain, fever, gastrointestinal disorders, ophthalmic diseases, hepatic disorders, renal diseases, respiratory disorders, immunological diseases, bone metabolism dysfunctions, central and peripheral nervous system diseases, sexual dysfunctions, infectious dis eases, for the inhibition of platelet aggregation and platelet adhesion, for treating pathological conditions resulting from abnormal cell proliferation , vascular diseases.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 2 125 695	30-Jan-2008	26-Oct-2016	30-Jan-2028
	U.S.	US 9,266,820	30-Jan-2008	23-Feb-2016	30-Jan-2028
	Canada	CA 2,677,387	30-Jan-2008	21-Jun-2016	30-Jan-2028

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 125 695 was validated in FR, DE, IT, GB and ES

Nitric Oxide Donating NSAIDs

Patent title: NITROSATED NON-STEROIDAL ANTIINFLAMMATORY COMPOUNDS, COMPOSITIONS AND METHODS OF USE

The patent family covers nitrosated nonsteroidal anti-inflammatory drugs (NSAIDs), compositions comprising a nitrosated NSAID and one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or at least one therapeutic agent.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date
Granted	U.S.	US 8,304,409	11-Dec-2009	06-Nov-2012	03-July-2023
	U.S.	US 8,222,277	28-Dec-2010	17-July-2012	03-July-2023
	U.S.	US 7,163,958	03-July-2003	16-Jan-2007	03-July-2023
	U.S.	US 7,754,772	23-May-2005	13-July-2010	03-July-2023
	U.S.	US 7,883,714	11-Dec-2009	08-Feb-2011	03-July-2023
	U.S.	US 8,088,762	11-Dec-2009	03-Jan-2012	03-July-2023

Nitric Oxide Donating NSAIDs

Patent title: PHARMACEUTICAL FORMULATION OF NITROOXYDERIVATIVES OF NSAIDs

The patent family covers pharmaceutical formulations in the form of gelatin capsules comprising a NO-releasing NSAID, one or more surfactants, a p-amino-phenyl-carboxylic acid derivatives of formula H_2N-$(CH_2)_m$-(C_6H_4)-COOH (m = 0-10) as carbonyl scavenger and optionally an oil or semi-solid fat and/or a short-chain alcohol. This patent family covers the Naproxcinod's formulation.

Patent owner: Nicox SA

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 8,691,869	29-Jun-2006	08-Apr-2014	28-July-2028
	Japan	JP 5238499	29-Jun-2006	05-Apr-2013	29-Jun-2026
	Canada	CA 2,616,508	29-Jun-2006	24-Feb-2015	29-Jun-2026
	Russian Federation	RU 2406482	29-Jun-2006	20-Dec-2010	29-Jun-2026

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations

Nitric Oxide Donating NSAIDs

Patent title: METHOD FOR TREATING VASO OCCLUSIVE CRISES ASSOCIATED WITH SICKLE CELL DISEASE

The patent family covers a method for treating vaso-occlusive crisis (VOC) associated with Sickle cell disease by administering a therapeutically effective amount of Naproxcinod.

Patent owner: Nicox SA

Patent status	Territory	Patent n°/ Publication n°	Filing Date	Issue Date	Expiry date*
Pending	U.S.[#]	US 2021/0244699	08-Feb-2021	-	08-Feb-2041
	Europe	EP 4 103 171	08-Feb-2021	-	08-Feb-2041
	Japan[§]	NA	08-Feb-2021	-	08-Feb-2041
	China[§]	NA	08-Feb-2021	-	08-Feb-2041
	Canada	CA 3,167,343	08-Feb-2021	-	08-Feb-2041

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) These patent applications are national/regional phases of the PCT application published as WO 2021/160543; the publication numbers are not available yet.
(#) US 2021/0244699 was filed in the name of Nicox SA and Fera Pharmaceuticals LLC

Triamcinolone acetonide nanocrystals Form C

Patent title: PREPARATION OF HYDROPHOBIC THERAPEUTIC AGENTS, METHOD OF MANUFACTURE AND USE THEREOF

The patent family covers a method for the preparation of triamcinolone acetonide (TA) Form C nanocrystals, pharmaceutical compositions comprising TA nanocrystals and methods for treating skin diseases (eczema, atopic dermatitis etc.) and allergic rhinitis and asthma.

Patent owner: Nicox Ophthalmics Inc.

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	Europe§	EP 2 941 437	13-Nov-2013	05-Sept-2018	13-Nov-2033
	U.S.	US 9,815,865	13-Nov-2013	14-Nov-2017	31-Dec-2033
	Canada	CA 2,897,670	13-Nov-2013	06-Apr-2021	13-Nov-2033

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations
(§) EP 2 941 437 was validated in FR, IT, DE, ES and GB

Triamcinolone acetonide nanocrystals Form B

Patent title: PREPARATION OF HYDROPHOBIC THERAPEUTIC AGENTS, METHOD OF MANUFACTURE AND USE THEREOF

The patent covers a method for the preparation of triamcinolone acetonide (TA) Form B nanocrystals, pharmaceutical compositions comprising the TA nanocrystals and methods for alleviating symptoms of blepharitis, postoperative ocular inflammation, dry eye or eye allergy and COPD, rhinitis and asthma.

Patent owner: Nicox Ophthalmics Inc.

Patent status	Territory	Patent n°	Filing Date	Issue Date	Expiry date*
Granted	U.S.	US 9,822,142	07-Jan-2013	21-Nov-2017	07-Jan-2033

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations

1.2.4. Competition

1.2.4.1. Overview

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We believe that our internally developed NO-donating- research platform, knowledge, experience and scientific resources provide us with competitive advantages. However, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our potential competitors include large pharmaceutical and biotechnology companies, and specialty pharmaceutical and generic drug companies. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of our potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient recruitment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of each of our product candidates, if approved for marketing, are likely to be its efficacy, safety, method of administration, convenience, price, the level of generic competition and the availability of coverage and adequate reimbursement from government and other third-party- payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Our product candidates target markets that are already served by a variety of competing products based on a number of active pharmaceutical ingredients. Many of these existing products have achieved widespread acceptance among physicians, patients and payors for the treatment of ophthalmic diseases and conditions. In addition, many of these products are available on a generic basis, and our product candidates may not demonstrate sufficient additional clinical benefits to physicians, patients or payors to justify a higher price compared to generic products. In many cases, insurers or other third-party- payors, particularly Medicare, seek to encourage the use of generic products. Given that we are developing products based on FDA approved therapeutic agents, our product candidates, if approved, will face competition from generic and branded versions of existing drugs based on the same active pharmaceutical ingredients that are administered in a different manner, such as biodegradable drug product formulations.

Because the active pharmaceutical ingredients in some of our product candidates are available on a generic basis or are soon to be available on a generic basis, competitors may be able to offer and sell products with the same active pharmaceutical ingredient as our products so long as these competitors do not infringe our patents.

Intellectual property covering certain other products such as ZERVIATE and NCX 4251 relate to the formulation and method of use of their active pharmaceutical ingredients. As such, if a third party were able to design around the formulation and process patents that we hold and to create a different formulation using a different production process not covered by our patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

1.2.4.2. Reduction of IOP in patients with glaucoma and ocular hypertension

Prostaglandin analogs are used as first line IOP lowering therapy and account for more than 50% of prescriptions for IOP lowering drugs in the U.S., where the leading branded product by sales is LUMIGAN (bimatoprost ophthalmic solution) 0.01% from Allergan, the other leading branded product is TRAVATAN Z (travoprost ophthalmic solution) 0.004% from Novartis, and the leading generic product is latanoprost. Generic travoprost and generic bimatoprost 0.03% are also available. ROCKLATAN (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%, a fixed dose combination of netarsudil and latanoprost, was also approved by FDA and subsequently launched in the U.S. in 2019 by Aerie Pharmaceuticals (acquired by Alcon in 2022). It was also approved in Europe in January 2021, under the brand name ROCLANDA. XELPROS (latanoprost ophthalmic emulsion) 0.005% was approved for IOP lowering in patients with open-angle glaucoma or ocular hypertension and was launched in the U.S. by a subsidiary of Sun Pharmaceutical Industries Ltd in 2019. Allergan, Inc., an Abbvie company, launched DURYSTA, a bimatoprost extended-release biodegradable implant for IOP lowering, in the U.S.in 2020. The other products in the market, currently used mostly as adjunct therapies added on the top of PGAs, are alpha agonists, beta blockers and carbonic anhydrase inhibitors, most of which are available as generic as well as branded forms. Another adjunct therapy, Rhopressa (netarsudil ophthalmic solution) 0.02%, a rho kinase inhibitor, was approved by FDA and launched in the U.S.by Aerie in 2018 and was approved under the brand name Rhokiinsa in Europe in 2019. OMLONTI, an EP2 agonist for IOP reduction that was launched in Japan under the brand name EYBELIS by the Japanese company, Santen, was approved in the U.S. in September 2022.

Several competitors are developing new formulations, novel chemical compounds and other sustained drug release products for the same ophthalmic indications as our current NO-donating compounds for IOP lowering.

The list below sets out the principal programs in Phase 3 (excluding generics of existing, approved products):

- *Glaukos* completed the clinical development of the iDose implant, which is a nonbiodegradable metal insert that releases travoprost and is placed in the eye during a surgical procedure. A New Drug Application in the U.S. is under preparation.
- Several drop-shaped presentations of latanoprost are in development or approved, for example, IYUZEH, a preservative-free formulation, approved in the U.S. in 2022 by Théa.

1.2.4.3. Competitors to our other products and product candidates

We may also be exposed to potentially competitive products which may be under development for our other indications.

Allergic conjunctivitis

The allergic conjunctivitis market is dominated by Alcon Laboratories, Inc.'s PAZEO, PATANOL and PATADAY, three products based on olopatadine at different concentrations, as well as generics of Olopatadine. Olopatadine is now also available as a non-prescription drug in the U.S., including some branded products The supplemental NDA for Ocular Therapeutix' DEXTENZA, a dexamethasone insert, for the treatment of ocular itching associated with allergic conjunctivitis, was approved in October 2021.

The list below sets out the principal programs in Phase 3 (excluding generics of existing, approved products):

- *Aldeyra Therapeutics, Inc.,* is in Phase 3 clinical trials with reproxalap (ADX102) for allergic conjunctivitis.
- *Faes Pharma,* has completed a Phase 3 clinical trial in the U.S. with bilastine for allergic conjunctivitis.

Dry Eye Disease

The principal prescription treatments for dry eye disease are RESTASIS (cyclosporine ophthalmic emulsion), 0.5%, from Allergan for which a generic has recently become available, XIIDRA (lifitegrast ophthalmic solution), 5%, from Novartis and CEQUA (cyclosporine ophthalmic solution), 0.09%, from Sun Pharmaceutical Industries. Products recently launched include EYSUVIS (loteprednol etabonate ophthalmic suspension), 0.25%, from Kala Pharmaceuticals and TYRVAYA (varenicline solution) nasal spray from Oyster Point Pharmaceuticals. Alcon Inc has acquired EYSUVIS and Viatris acquired Oyster Point Pharmaceuticals. The condition is also treated with non-prescription products, principally artificial tears.

The list below sets out the principal programs in Phase 3 (excluding generics of existing, approved products):

- *Palatin Technologies* is developing PL9643 ophthalmic solution, currently in a Phase 3 clinical trial for dry eye disease.
- *RegenTree* is developing RGN-259 ophthalmic solution, containing Thymosin beta 4, currently in a Phase 3 clinical trial for dry eye disease.
- *Hanal BioPharma Co., Ltd.* and *Daewoong Pharmaceutical Co. Ltd* are developing tanfanercept (HL036) ophthalmic solution 0.25%, currently in a Phase 3 clinical trial for dry eye disease.
- *Aldeyra Therapeutics* is developing Reproxalap Ophthalmic Solution (0.25%), a RASP inhibitor. An NDA in the U.S. is under preparation.
- *Novaliq GmbH* is developing CyclASol Ophthalmic Solution (cyclosporine) for which Novaliq has filed an NDA in the U.S. in 2022 and an innovative product, the partially fluorinated alkane, NOV03 (perfluorohexyloctane), for which an NDA in the U.S. has also been filed in 2022 by its partner, Bausch + Lomb.
- *Mitotech* has completed a Phase 3 trial on SkQ1 ophthalmic solution for dry eye disease.
- *Senju Pharmaceutical* is developing SJP-0132, dry eye drops, into Phase 3 in Japan.
- *Senju Pharmaceutical* is developing SJP-0035, dry eye drops, in Phase 3 in Japan.
- *Aerie Pharmaceuticals (acquired by Alcon)* is developing acoltremon (AR-15512, AVX-012, WS-12), an ophthalmic formulation of a transient receptor potential (TRP)M8 agonist, in Phase 3 for dry eye disease in the U.S.
- *Allysta Pharmaceuticals* is developing an ophthalmic formulation of ALY-688, a synthetic peptide analog of adiponectin that acts as an agonist of the adiponectin receptor, in Phase 3 for dry eye disease in the U.S.
- *Santen* filed an NDA in Japan in 2022 for STN-1013500, in development in dry eye disease.
- *Kowa* is developing K-161, in Phase 3 for Phase 3 for dry eye in Japan.

- Several other formulations of the active ingredient of the active ingredient cyclosporine are in development for dry eye.

1.2.4.4. Other NO-delivery and NO-donating technologies in ophthalmology

As far as we are aware, there are at two pharmaceutical companies working in the field of NO-donating- drugs in ophthalmology:

- *Kowa Pharmaceutical Europe Co. Ltd.* markets HYPADIL Kowa Ophthalmic Solution 0.25% in Japan for the treatment of glaucoma and intraocular hypertension. The active ingredient of this drug is nipradilol, an alpha and beta--adrenergic blocker with NO--releasing- action.
- *Topadur* is developing an NO-releasing PDE5 inhibitor in retinal conditions at a preclinical stage.

It is important to note that once marketed (subject to obtaining marketing approvals on an ad hoc- basis), the products developed by us will be competing with a number of products that are already commercially available. In addition, research conducted by the pharmaceutical industry and by public and private institutions will continue to generate new products that could compete with our existing or future commercial products.

1.2.5. Investments

The Company has not made any investments since January 1, 2022.

1.2.5.1. Historical investments

The Company subcontracts its research, development, and production activities for the active ingredient of its drugs and therefore the tangible fixed assets are not significant compared to the overall research and development expenses of the Company. The gross value of property, plant and equipment amounts to € 2,602,000 as of December 31, 2022.

The Company's intangible assets mainly break down as follows:

- A portfolio of unlicensed patents acquired in April 2009 from the Nitromed Company, covering nitric oxide donor compounds with a gross value of €2,000,000.

- The late-stage drug pipeline targeting major segments of the ophthalmology market of Nicox Ophthalmics Inc. (formerly Aciex Therapeutics Inc.) for a gross amount of €76,599,725.

1.2.5.2. Ongoing investments

The Company has no significant investments in progress.

1.2.5.3. Environmental information that may influence the use made by the Company of its property, plant and equipment

In accordance with the MiddleNext corporate governance code updated in September 2021 to which the company refers and the internal regulations of the Board of Directors, the Corporate Governance Committee and then the Board of Directors examined the social, societal, and environmental consequences. of the Company's activities and strategy. The Board of Directors considered that the activities and strategy of the Company do not have significant consequences which would require specific action.

The Group only has offices with limited environmental impact. In addition, the Group's subcontracted activities are, for the most part, intellectual activities with a moderate impact on the environment, the other subcontracted activities (in particular research and development activities) being limited in terms of their impact on the environment. terms of financial flows at the date of publication of this report.

The Group is not subject to specific environmental certification procedures.

There are no provisions and guarantees for environmental risks.

The Group did not pay any compensation during the financial year in execution of a court decision in environmental matters.

2. Presentation of group results and key performance indicators

2.1. Income statement and balance sheet highlights

The 2022 consolidated financial statements, as adopted by the Board of Directors on April 28, 2023, were certified by the Statutory Auditors.

Changes in the Group's consolidation perimeter are described in the note 3.1 of the consolidated accounts.

2022 financial results

Net revenue[1] for the full year 2022 was €3.3 million (consisting entirely of net royalties), compared to €7.2 million (€2.4 million in net royalties, €4.8 million in partnership license payments) for the full year 2021.

Operating expenses for the year 2022 increased to €27.2 million from €25.1 million for the previous year.

Nicox Group reported a net loss for 2022 of €27.8 million down from €43.8 million from the prior year. This included €10.9 million of non-cash items resulting from an additional reduction in the estimated fair value of NCX 4251 following the Group's decision not to pursue internal development but to seek a partner in the U.S. The 2021 net loss included €27.8 million of non-cash items due to a reduction in the estimated fair value of ZERVIATE (of €12.7 million) and of NCX 4251 (of €15.1 million) reflecting, respectively, the changes in the allergic conjunctivitis market in the U.S. and the changes in the development plan and timeline for NCX 4251.

As of December 31, 2022, the Nicox Group had cash and cash equivalents of €27.7 million as compared with €42.0 million at December 31, 2021. As of December 31, 2022, the Nicox Group had cash and cash equivalents of €27.7 million, as compared with €42.0 million as of December 31, 2021.

As of December 31, 2022, the Nicox Group had financial debt of €24.7 million, consisting of (i) €18.7 million in the form of a bond financing agreement with Kreos Capital signed in January 2019, (ii) a €1.8 million credit agreement guaranteed by the French State, and granted in August 2020 in the context of the COVID-19 pandemic and (iii) €4.2 million of present value attributed to the put option granted in the November 2022 equity financing. The payment of this debt would only occur if the put option was exercised, subject to the following conditions: In the case of a mergers by absorption or by the creation of a new company control, a spinoff or a change in control within the meaning of article L. 233-3 I of the French commercial code (*Code de commerce*) where the consideration for such transaction is Nicox shares at a value of less than €1.70, the exercise price of the warrants, Armistice can request that Nicox purchases the warrants granted to Armistice at their Black Scholes value (using pre-defined terms). The present value of this option is revised at each closure and the non-cash adjustment of the present value is recognized in the consolidated statement of profit or loss as a finance income or finance expense.

[1] Net revenue consists of revenue from collaborations less royalty payments which corresponds to net profit in the consolidated statement of profit or loss.

Principal consolidated financial data

CONSOLIDATED STATEMENT OF PROFIT OR LOSS

In €000	For the period ended December 31	
	2022	2021
Revenue from collaborations	**5,242**	**8,583**
Royalty payments	(1,971)	(1,350)
Net profit*	**3,271**	**7,233**
Research and development expenditures	(17,992)	(17,910)
Administrative expenses	(7,479)	(7,000)
Other income	762	843
Other expenses	(1,753)	(211)
Operating loss before amortization and impairment of intangible assets	**(23,191)**	**(17,045)**
Amortization of intangible assets		(1,205)
Impairment of intangible assets [1]	(10,870)	(27,760)
Operating loss	**(33,959)**	**(46,010)**
Financial income [2]	6,062	3,456
Finance expenses [3]	(2,288)	(4,851)
Net financial income/(expense)	**3,774**	**(1,395)**
Loss before tax	**(30,287)**	**(47,405)**
Income tax (expense) / benefit	2,528	3,644
Loss after tax	**(27,759)**	**(43,761)**
Loss for the period	**(27,759)**	**(43,761)**

(1) Includes in 2022 an additional non-cash adjustment on NCX 4251 fair value, decreasing by €(10.9) million due to the decision to seek a partner to pursue the development of NCX 4251 in the U.S. Includes in 2021 two non–cash adjustments on U.S. ZERVIATE estimated fair value decreasing by €(12.7) million, due to changes in the United States allergic conjunctivitis market, and on NCX 4251 estimated fair value, decreasing by €(15.1) million, reflecting the changes made to the development plan and timeline for NCX 4251.

(2) Includes in 2022 an income of €3.0 million related to the adjustment of the present value of the put option granted by Nicox to Armistice in the November 2022 equity financing. The amount of 3 million euros corresponds to the change in the present value of the option between the date of the financing and December 31, 2022.

(3) Includes in 2021 a net loss of €(3.3) millions related to the restructuration of the Kreos debt.

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

In €000	At December 31	
ASSETS	**2022**	**2021**
Non-current assets		
Goodwill	27,223	25,637
Intangible assets [(1)]	31,692	39,974
Property, plant and equipment	240	1,023
Non-current financial assets	325	237
Total non-current assets	**59,480**	**66,871**
Current assets		
Trade receivables	2,639	1,086
Government grants receivable	504	1,452
Other current assets	1,279	377
Prepayments	1,612	2,853
Cash and cash equivalents	27,650	41,970
Total current assets	**33,684**	**47,738**
TOTAL ASSETS	**93,164**	**114,609**
LIABILITIES		
Shareholders' equity		
Issued capital	50,100	43,138
Share premium	538,202	536,200
Translation reserve	7,665	5,953
Treasury shares	(978)	(847)
Accumulated deficit	(542,556)	(508,892)
Total equity	**52,433**	**75,552**
Non-current liabilities		
Non-current financial liabilities [(2)]	24,606	21,160
Deferred tax liabilities	7,341	9,236
Provisions	578	661
Total non-current liabilities	**32,525**	**31,057**
Current liabilities		
Current financial liabilities	828	346
Trade payables	3,102	3,649
Deferred income	2,183	1,970
Other current liabilities	2,093	2,035
Total current liabilities	**8,206**	**8,000**
TOTAL EQUITY AND LIABILITIES	**93,164**	**114 609**

(1) Includes in 2022 an additional non-cash adjustment on NCX 4251 fair value, decreasing by €10.7 million due to the decision to seek a partner to pursue the development of NCX 4251 in the U.S.

(2) Includes in 2022 €4.1 million of present value of the put option granted by Nicox to Armistice in the November 2022 equity financing.

Statutory disclosures on the AR/AP aged trial balance

As the Company does not have direct sales, there is no reason to provide information on the aged trial balance for accounts receivable..

Statutory disclosures on the accounts payable aged trial balance at December 31, 2022 are presented below by due date:

	Invoices received and not settled on the closing date and past due					Invoices issued and not settled on the closing date and past due					
	0 day (indicative)	1 to 30 days	31 to 60 days	61 to 90 days	91 days or more	Total (1 day and more)	0 day (indicative)	1 to 30 days	31 to 60 days	61 to 90 days	91 days or more	Total (1 day and more)
(A) Late payment date ranges												
Number of invoices concerned	92					**9**	2					**3**
Total amount of concerned invoices incl. VAT	744,545	4,408	-	399	5,554	**10,362**	368,571	-	516,184	-	-	**516,184**
Percentage of total purchases of the period incl. VAT	3.466%	0.021%	0.00%	0.002%	0.026%	**0.048%**						
Percentage of revenue of the period incl. VAT							4.49%	-	6.29%	-	-	**6.29%**
(B) Invoices excluded from (A) relating to disputed or unrecognized payables and receivables												
Number of invoices					6	**6**						
Amount of invoices					5,364	**5,364**						

Research and development

The Group's research and development programs are described in Section 1.2.1.4 "Company's portfolio".

Nicox's Research and Development activities are organized in such a way as to achieve efficient product development with a maximum flexibility and the rational use of resources.

The outsourced share of research and development work at December 31, 2022 accounted for 74.5% of total spending on research and development by the Company.

Intellectual property related activities (patents) are managed by Nicox Research Institute Srl.

Research and development expenditures by project

The following table summarizes research and development expenditures incurred by the Company by project or patent family, before taking into account contingent consideration for the last two financial periods.

	At December 31	
	2022	2021
	In €000	
Internal expenditures	4,370	4,031
External expenditures	13,406	13,619
ZERVIATE	*63*	*100*
NCX 4251	*496*	*3,918*
*NCX 470**	*11,792*	*8,804*
Other expenses not allocated by project	*1,055*	*797*
Other expenditures	217	260
Total R&D expenditures	**17,992**	**17,910**

* Deduction of expenses charged back to Ocumension relating to the Denali study

Summary of expenses linked to patent filings and managing our patent portfolio included in our research and development expenditures is presented in the above table:

In €000	FY	
	2022	2021
Expenses linked to the patent portfolio	613	558

Current investments

The Company has no significant current investments.

2.2. Cash flows

2.2.1. Cash flows from operating activities.

In 2022, net cash flow used in operating activities represented outflows of €23.1 million compared to €18.5 million in 2021. Operating research and development expenditures remained stable in 2022 compared with the prior year. In 2021, the Company received €4.8 million in non recurring milestone payments which reduced net cash requirements for the year.

2.2.2. Cash flows from investing activities.

Cash flows from investing activities in 2022 and 2021were not significant.

2.2.3. Cash flows from financing activities.

Cash flows from financing activities amounted to €8.6 million in 2022 compared to €13.4 million in 2021 and resulted mainly from a capital increase through the issuance of new shares to institutional investors in 2021 generating net proceeds of €9.0 million. In 2021, net cash from financing activities was mainly due to a €13.8 million equity issue to institutional investors.

Information concerning the issuer's capital resources (both short term and long term)

Since its Initial Public Offering, the Company has financed itself mainly by raising funds through private and public placements on Euronext. To date, the Company has earned little revenue from the sale of pharmaceuticals, medical devices and nutraceuticals in ophthalmics in Europe and international markets from 2013 until August 2016, the date these operations were transferred. Nicox also receives payments from strategic partners in connection with collaboration agreements though these payments are not sufficient to cover operating expenses.

Accordingly, in March 2010, Bausch + Lomb (an affiliate of the Valeant group) entered into a worldwide licensing agreement with Nicox for latanoprostene bunod and has made to date three milestone payments to Nicox totaling $22.5 million, after deducting amounts paid to Pfizer under the terms of the agreement executed in 2009 by which Nicox recovered the rights to latanoprostene bunod previously licensed to the former. Following the commercial launch of VYZULTA (latanoprostene bunod ophthalmic solution), 0.024% in December 2017, the Company receives royalties on net sales after deducting payments to Pfizer. Net royalties may reach 12% net in the future. The Company will also receive contingent consideration for regulatory milestones and commercial objectives for a total of US$150 million after deducting amounts payable to Pfizer.

In 2017, Nicox also entered into a license agreement with Eyevance for the marketing of ZERVIATE in the United States. On that basis, it received an initial payment of US$6 million in 2017 and a milestone payment of €3 million dollars in 2019. In the future, Nicox may receive up to US$37.5 million in contingent consideration based on regulatory and business objectives as well as royalties of 8% to 15% based on ZERVIATE's future net sales. The Group has also undertaken to pay Eyevance US$502,000, linked to the manufacturing costs resulting from delays in completing certain activities. This amount became payable after achieving royalty payments from Eyevance and is directly deducted from these royalties. The outstanding balance at December 31, 2021 was €367,000

In December 2018, the Company entered into an exclusive license agreement with Ocumension Therapeutics, an international ophthalmology company. The agreement concerns the development and commercialization of its NCX 470 drug candidate, targeting patients with glaucoma or ocular hypertension for a territory comprising mainland China, Hong Kong, Macau, and Taiwan. Under the terms of this agreement, the company received in December 2018 a one-time upfront payment of €3 million and may receive €33.25 million in milestone payments associated with progress of NCX 470 up to regulatory approval and commercial objectives. The Company will also receive tiered royalties from 6% to 12% on sales.

In March 2019, Nicox entered into an exclusive licensing agreement with Ocumension for the development and commercialization in the Chinese market of its product, ZERVIATE® for the treatment of allergic conjunctivitis. Nicox granted Ocumension exclusive rights to develop and commercialize ZERVIATE, at its own costs, in the agreed territory. In March 2020, Nicox s amended its license agreement with Ocumension Therapeutics, under which Ocumension has exclusive rights to develop and commercialize ZERVIATE® in the Chinese and the majority of South East Asian markets. Under the amended agreement of July 2021, Ocumension paid Nicox $2 million in full advance payment of the future development and regulatory milestones for the product. Nicox remains eligible to receive the same sales milestones of up to US$17.2 million together with tiered royalties of between 5% and 9% of net sales of ZERVIATE by Ocumension. Ocumension submitted a New Drug Application (NDA) was submitted in April 2023 for approval to commercialize ZERVIATE in China. The application was granted priority review status by the National Medical Products Administration of the People's Republic of China (NMPA) which should accelerate the approval process and the commercial launch of ZERVIATE in China expected in 2024.

In June 2019, the Company entered into an exclusive license agreement with Ocumension for the development and commercialization of its drug candidate, NCX 4251 for a territory covering continental China, Hong Kong, Macao and Taiwan. Ocumension is responsible, at its own cost, for all development activities necessary for the

approval of NCX 4251 in the relevant territory. Ocumension was granted exclusive rights for the agreed territory to develop and commercialize NCX 4251 for blepharitis. Under the terms of the agreement, the Company received an initial payment of US$2.3 million and may potentially receive development and sales milestone payments of up to US$11.3 million together with tiered royalties of between 5% and 10% on sales of NCX 4251.

In December 2019, the Company signed an exclusive license agreement with Samil Pharmaceutical Co., Ltd for the development and commercialization of ZERVIATE™ (cetirizine ophthalmic solution), 0.24% for the treatment of ocular itching associated with allergic conjunctivitis in South Korea. Nicox thus granted Samil Pharmaceutical exclusive rights to develop and commercialize ZERVIATE in South Korea. Nicox is eligible to receive 10% royalties on net sales on ZERVIATE in South Korea and a milestone payment of 5% of net sales for each calendar year in which net sales exceed approximately US$900,000. Nicox received a significant license fee upon the signature of the agreement, and may receive in addition approval and launch milestone payments which may total approximately US$189,000. Samil Pharmaceutical will be responsible, at its cost, for the development and commercialization of ZERVIATE in South Korea. ZERVIATE is expected to require manufacturing transfer and associated pharmaceutical development to support approval in South Korea, in addition to the existing approved U.S. NDA package.

In March 2020, Nicox signed an amendment to the license agreement with Ocumension for NCX 470. Under the amended agreement, Ocumension paid Nicox €15 million (€14 million of which is repayable under certain conditions), replacing in full the milestone payments under the original agreement. Under the amended agreement, Ocumension gained additional exclusive rights to NCX 470 for Korea and South East Asia and undertakes to pay 50% of the costs of the second glaucoma Phase 3 clinical trial of NCX 470 ("Denali"). The two companies jointly manage the Denali trial in the U.S. and China. No future NCX 470 milestones will be due from Ocumension to Nicox. In the unlikely case that the Joint Trial would not take place, partial refunds may be made and in certain situations the original milestones of the agreement would again apply. The tiered royalties of 6% to 12% of the original agreement remain unchanged and will apply to sales in the original and the additional territories.

In August 2020, ITROM was granted exclusive rights to develop and commercialize ZERVIATE in Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Oman, Qatar, the Kingdom of Saudi Arabia, the United Arab Emirates and Yemen. Nicox is eligible to receive 15% royalties on net sales of ZERVIATE in certain key countries, and 10% in other countries. Nicox will also receive a non-significant license fee on signature and may receive a future milestone payment upon the product launch of ZERVIATE. ITROM will be responsible, at its own cost, for development and commercialization of ZERVIATE in the countries of the agreement. ZERVIATE is expected to require only the existing approved U.S. New Drug Application (NDA) package to support approval.

In January 2019, the Company obtained financing from Kreos Capital for up to €20 million structured as bonds and consisting of 3 tranches. These tranches were all subscribed for in 2019, while the funds of the last tranche were however not received until January 2, 2020.

After being restructured in November 2021 this loan agreement now includes a bond component convertible into shares amounting to €3.3 million. Nicox also obtained and 2020, a €2.0 million French State guaranteed loan in connection with measures made in response to the Covid-19 pandemic. In addition, the Company raised €15 million in gross proceeds from a private placement with institutional investors in December 2021.

In November 2022, the Company raised €10 million in gross proceeds and exercised the option to extend the interest-only payment period and the maturity date of the loan for an additional 6 months to January 2024 and July 2026, respectively, as the Mont Blanc Phase 3 clinical trial for NCX 470 met its primary endpoint of non-inferiority to latanoprost before July[1,] 2023. These two transactions extended the cash runway to mid-May 2024.

At December 31, 2022, Nicox's consolidated cash and cash equivalents amounted to €27.7 million compared to €42.0 million at December 31, 2021.

In the future, Nicox may be led to seek out new sources of financing either through a capital increase or through other forms of financial debt for multiple reasons, including in particular the costs of development, acquisitions, and the registration of products under development.

The following table summarizes the main equity financing operations of the Company on the date of the Annual Report (gross proceeds in €m):

TYPE OF TRANSACTION	1996	1997	1999	2001	2004	2006	2007	2009	2015	2016	2017	2019	2020	2021	2022	Total
Venture Capital	2	6.3														8.3
Initial public offering (Paris)			33.2													33.2
Offer				59.3			130	69.9								258.9
Private investment in a public entity (PIPE)					26	45.5		30.5	27	18	26.3	12.5	15	15	10	215.8
Private investment in a public entity (PIPE) – Pfizer							15									15
TOTAL	**2**	**6.3**	**33.2**	**59.3**	**26**	**45.5**	**145**	**100**	**27**	**18**	**26.3**	**12.5**	**15**	**15**	**10**	**546.2**

The sources and amounts of and a narrative description of the issuer's cash flows

Historically, the company financing capital has been derived from capital increases for a specific category of investors or public offerings, payments received from partners in connection with license agreements and research tax credits. In addition, the Company entered into a loan agreement in January 2019 that was amended in 2021. In 2020 the Company also obtained out a French State-guaranteed loan. The corresponding terms and conditions are described below in the section "Borrowing requirements and funding structure".

Information on the financing needs and funding structure of the Company

In the 2020 third quarter, the Group obtained loan agreements guaranteed by the French State (up to 90%) from Société Générale and LCL for an amount totaling €2 million in the context of the COVID-19 pandemic. These loans, unsecured by Group assets, with an initial maturity of 12 months, were extended by a further 12 months. The period for repayment is five years beginning in August 2022. The bond financing agreement with Kreos Capital VI (UK) Limited executed on January 29, 2019 for €20 million and amended in January 2021 with respect to the repayment period of the principal was subject to a new amendment dated November 30, 2021 (the Amendment). Prior to the signature of this Amendment, the nominal amount of the debt with Kreos Capital amounted to €16.9 million. The amendment executed on November 20, 2021 introduced the following changes (with the other terms of the original contract remaining unchanged): (i) the maturity period of the loan was extended by 18 months, i.e. until January 1, 2026, with the Company benefiting from an option to extend this period by 6 months (i.e. until July 1, 2026) if the clinical study of the Mont-Blanc study meets the primary endpoint of non-inferiority compared to latanoprost before June 2023 and (ii) the Company will also benefit from an extension of the interest-only payment period to August 1, 2023, which may be extended by an additional 6 months (to February 1, 2024) at the Company's option and subject to the same condition relating to the Mont Blanc study. The Amendment also provides for prepayment, without penalty, of 30% of the bond

principal, i.e., €5,087,347, on its date of effect. This amount was transferred by Kreos Capital VI (UK) Limited to Kreos Capital VI (Expert Fund) L.P., to subscribe by way of offset to an issue of bonds convertible into new shares (the "Convertible Bonds"), reserved for subscription by Kreos Capital VI (UK) Limited (the "Convertible Bond Issue "). The convertible bond issue consisted of 3,300,000 bonds with a nominal value of 1 euro each, conferring entitlement to a maximum of 900,000 new shares with a nominal value of 1 euro each if converted into shares (able to be converted at any time, subject to a non-conversion period of 60 days from the date of issue). The conversion ratio for the Convertible Bonds into shares corresponds to a price of €3.67 or a 25% premium over the VWAP calculated on the 3-days trading preceding the date of the Board of Directors' meeting determining the final terms of the Convertible Bond Issue. The Convertible Bond Issue is secured by the collateral in place for the Bond Issue Agreement. The interest rate (9.25% per annum) and maturity are identical to those of the pre-existing debt issue. Should Kreos Capital VI (Expert Fund) L.P. fail to convert the bonds on maturity of the Convertible Bond Issue, the entire amount of the Convertible Loan remaining will be due as a single payment at that time. The remaining €1,787,347 under the Kreos Capital VI (Expert Fund) L.P.'s debt financing agreement were used to subscribe for the issue of new non-convertible bonds bearing an interest of 9.25%, with the same maturity as the Convertible Bond Issue and with an additional premium payable upon redemption, so that the total return to Kreos Capital VI (Expert Fund) L.P. is 1.75 times the initial amount of capital. This premium was recorded in the parent company financial statements and will be amortized over the remaining term of the loan. The Amendment also provided for the payment to Kreos by the Company of a restructuring commission of €339,156.44.

In November 2022, the Company exercised the option to extend the interest-only payment period and the maturity date of the loan for an additional 6 months to January 2024 and July 2026, respectively, as the Mont Blanc Phase 3 clinical trial for NCX 470 met its primary endpoint of non-inferiority to latanoprost before July[1,] 2023. This option does not apply to the convertible bonds with a nominal amount of €3.3 million or the non-convertible bonds with a nominal amount of €1.8 million, whose maturity date, including premium, remains January 1, 2026.

This extension has deferred repayment of the principal due for the period from August1, 2023 to February 1, 2024 in the amount of €2.1 million. This repayment will now be made from February 1, 2024 to July 1, 2026. This option to extend the loan by a further six months resulted in an additional interest payment of €0.8 million in 2026.

Information concerning no restrictions on the use of capital resources that have materially affected or could materially affect, directly or indirectly, the Company's activities.

The pledges given for the bond issue described above could limit the use of the Company's capital resources in the event of a default in the payment of this debt. In such case, this restriction would adversely affect the good conduct of the Company's business (see section 2.7.1.1 “Risks relating to cash burn”).

Information concerning anticipated sources of funds required to honor material investments of the Company in progress or for which firm commitments have already been made

The tangible fixed assets of the Company are not significant. Should the Company decide to embark on investment projects, their funding would be explored case-by-case on an ad-hoc basis. This may involve securities-backed or cash financing, or the transfer of assets already owned by the Company. In the first two instances, the Company will make capital increases pursuant to resolutions passed by the extraordinary general meeting in force.

2.3. Annual highlights

2.3.1. Governance / Board of Directors

Change of Chief Executive Officer

On May 13, 2022, the Company's Board of Directors decided to end Michele Garufi's term of office, the cofounder of the Company and Chairman and Chief Executive Officer since its creation in 1996, and to replace him with Andreas Segerros as Chief Executive Officer, effective June 1, 2022. Michele Garufi will remain as Board member of Nicox SA. The Board has also decided to separate the functions of Chief Executive Officer and Chairman of the Board and to entrust the chairmanship of the Board of Directors to Mr. Jean-François Labbé, Director and Chairman of the Audit Committee. This appointment required the approval of an amendment to the Company's articles of association (*statuts*) to increase the age limit for the Chairman of the Board granted by the Extraordinary General Meeting of July 28, 2022. Between June[1] and July 28, 2022, Michele Garufi served as Interim Chairman of the Board.

Change of Chairman of the Board of Directors

Jean-François Labbé, Director of the Company and Chairman of the Audit Committee, was appointed Chairman of the Board of Directors effective July 28, 2022. Mr. Michele Garufi, who remains a director, was Chairman and Chief Executive Officer until May 31, 2022 and then Interim Chairman of the Board between June1 and July 28, 2022.

The composition of the Board of Directors (s well as the conditions for the preparation and organization of its work) is described in Part 2 of this Annual Report.

2.3.2. Financing

November 2022 equity financing

On November 22, 2023, the Company announced new financing in the form of a private placement of 6,849,316 new ordinary shares with warrants attached (ABSA) for the subscription of 6,849,316 additional ordinary shares, at a price of €1.46 per share with a warrant exercisable at a price of €1.70. The growth proceeds from this issue amounted to €10 million or net proceeds of approximately €8.9 million, excluding the potential exercise of associated warrants.

2.3.3. Annual highlights (press releases)

January 5, 2022	Nicox European Patent Seals ZERVIATE Major Market Coverage to 2030
January 21, 2022	Nicox Provides Fourth Quarter 2021 Business and Financial Highlights
January 27, 2022	Nicox to Participate in Financial, Pharmaceutical Industry and Scientific Events in H1 2022
February 8, 2022	Nicox's Positive FDA Meeting Shows Clear Path for NCX 4251 in Dry Eye
February 21, 2022	Nicox Granted New Patent for NCX 470 in China, Extending Coverage to 2039
February 22, 2022	Nicox Granted New Patent for NCX 4251 in Japan
February 23, 2022	Nicox Announces VYZULTA Now Commercialized in 7 Territories and Approved in Further 9 Countries
March 1, 2022	Nicox's Partner Ocumension Obtains Positive Phase 3 Clinical Trial Results for ZERVIATE® in China

March 2, 2022	Nicox's Partner Fera Pharmaceuticals Obtains Orphan Drug Designation from the U.S. FDA for Naproxcinod for the Treatment of Sickle Cell Disease
April 11, 2022	Nicox's NCX 470 Dolomites Phase 2 Results Published in Journal of Glaucoma
April 28, 2022	Nicox Reports 2021 Financial Results and First Quarter 2022 Financial Highlights and Provides Update on Key Programs and Milestones
May 2 2022	Nicox at ARVO 2022: Presentation of clinical Phase 2 results on NCX 4251 and new non-clinical evidence of improved hemodynamic and retinal cell physiology on NCX 470
May 4, 2023	Nicox: 2022 Ordinary Shareholder Meeting
May 16, 2023	Nicox Announces a New Governance Structure
June 3, 2022	Nicox Accelerates Topline Results from NCX 470 Mont Blanc Phase 3 Glaucoma Trial to November 2022
July 7, 2022	Nicox Announces Publication of NCX 470 Results Demonstrating Improvements to Ocular Hemodynamics and Retinal Cell Physiology
July 20, 2022	Nicox Provides Second Quarter 2022 Financial and Business Highlights
July 29, 2022	Nicox Appoints Jean-Francois Labbé as Chairman of the Board of Directors
August 3, 2022	Nicox to Participate in Financial and Scientific Events in Q3 2022
September 16, 2022	Nicox Provides First Half 2022 Business Update and Financial Results
September 19, 2022	Nicox Announces Last Patients Complete Final Visit in NCX 470 Phase 3 Mont Blanc Glaucoma Trial
October 19, 2022	Nicox Provides Third Quarter 2022 Financial and Business Highlights
October 31, 2022	Nicox Reports Achieving Primary Objective in Mont Blanc, the First Phase 3 Glaucoma Trial for NCX 470
November 7, 2022	Nicox Outlines Future Development and Partnering Plans for NCX 470 in Glaucoma

2.4. Significant subsequent events

2.4.1. Transfer to Euronext Growth

The Company's Ordinary General Meeting of February 28, 2023 approved the proposed transfer of the listing of the Company's securities from the regulated market of Euronext Paris (compartment C) to the Euronext Growth Paris multilateral trading facility.

This market is better adapted for the trading of the Company's shares in relation to its size, market capitalization and the level of its free float. The transfer to Euronext Growth Paris will reduce the Company's obligations and constraints and, as a result, reduce the costs associated with its listing, while maintaining the shares' tradability on a financial market.

The application for admission of the Company's shares to Euronext Growth was approved by the Euronext Listing Board on April 24, 2023.

At the end of the trading session of April 27, 2023, the Company's shares were delisted from the regulated market of Euronext Paris and admitted to Euronext Growth Paris as of April 28, 2023.

As of April 28, 2023, the new ticker for Nicox SA shares is ALCOX. The ISIN code remains unchanged: FR0013018124 XPAR.

The main consequences of this transfer are set forth in note 30 to the consolidated financial statements for the year ended December 31, 2002, in Part 3 of this Annual Report.

2.4.2. Material subsequent events (press releases)

January 6, 2023	Half-year liquidity contract statement with Kepler Cheuvreux (as of December 31, 2022)
January 9, 2023	Nicox Announces Proposed Move to Euronext Growth Paris
January 18, 2023	Nicox Provides Fourth Quarter 2022 Financial Highlights
Jnauary 24, 2023	Nicox to Participate in Financial, Pharmaceutical Industry and Scientific Events in H1 2023
February 13, 2023	Nicox's Ordinary Shareholder Meeting to be held on February 28, 2023
March 1, 2023	Nicox: Ordinary Shareholder Meeting of February 28, 2023 – Approval of all Resolutions
March 3, 2023	Nicox to Present at Upcoming Scientific Conferences
March 20, 2023	Nicox Reports 2022 Financial Results and Updates Key Future Milestones
March 21, 2023	Nicox Announces Presentations of Additional NCX 470 Data at the Upcoming World Glaucoma Congress
April 14, 2023	Additional Future Royalty Revenue Stream for Nicox from 2024 following New Drug Application Submission for ZERVIATE in China
April 19, 2023	Nicox Provides First Quarter 2023 Financial and Business Highlights
April 24, 2023	Nicox: 2023 Ordinary Shareholder Meeting to be held on June 1, 2023
April 26, 2023	New Data on Two Nicox's Assets, NCX 470 and NCX 1728, Presented at ARVO 2023
April 26, 2023	Transfer of Nicox's shares to Euronext Growth Paris effective on April 28, 2023
April 28, 2023	Nicox's Partner Ocumension Therapeutics Receives Priority Review Status for ZERVIATE New Drug Application in China

2.5. Outlook / Trend Information

Significant events since January 1, 2023 are described in section 2.4 of this Annual Report.

The uncertainties surrounding the company's prospects and operations are described in section 2.7 of this Annual Report.

There have been no material changes with respect to the group's financial performance since the closing of fiscal year 2022.

2.6. Profit forecasts or estimates

The Company does not publish profit forecasts or estimates.

2.7. Risk factors and insurance

This section presents the key risks which on the date of this Annual Report could have a material adverse effect on its business, financial status, operating results, or ability to achieve its objectives. However, the occurrence of risks unknown on the date of this Annual Report or not considered likely to have a material adverse effect on

the date of this Annual Report cannot be excluded. Each year the Board of Directors reviews the risks to which the Company is exposed and issues an opinion as to their importance.

The key risks to which the Company considers it is exposed are presented according to the following categories, without any order of importance: (i) risks relating to the Company's financial position and capital requirements, (ii) risks relating to the products developed by the Company, regulatory authorizations and sale, (iii) risks relating to a dependence on third parties, (iv) risks relating to the Company's intellectual property, (iv) risks relating to the Company's organization, structure and operations, and (vi) risks relating to legal and administrative proceedings.

2.7.1. Risks relating to the Company's financial position and capital requirements

2.7.1.1. Risks associated with cash burn

At December 31, 2022 Nicox Group had cash and cash equivalents in the amount of € 27.7 million compared to €42.0 million at December 31, 2021.

Based on a specific review of its liquidity risk, Nicox considers that on the date of this Annual Report the Company has sufficient net working capital to meet its cash requirements until Q2 2024, based exclusively on the development of NCX 470. The second Phase 3 clinical trial, Denali, is expected to be achieved in 2025, therefore additional financing will be required to complete this trial. This date of 2025 is based on projections of increased recruitment which take notably into account the lifting of COVID-19 restrictions in China.

In addition to corporate structure costs, Nicox anticipates significant capital requirements to complete the following projects:

- The development program for NCX 470, a novel nitric oxide (NO)-donating bimatoprost eyedrop for lowering of intra-ocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension, by continuing to progress the Denali Phase 3 trial and completing the final activities in the Mont Blanc Phase 3 trial

- New Phase 3b clinical trials to investigate the NCX 470 dual mechanism of action (nitric oxide and prostaglandin analog) in IOP lowering and potential beneficial effects of NCX 470 on the retina

Development and the cost of clinical and non-clinical trials, as well as costs relating to research and development programs, filing patents and concluding collaboration or product manufacturing agreements also give rise to significant capital requirements that must be met by Nicox.

To date, limited revenues are generated from royalties derived from the direct sales of products. Nicox expects sales for 2023 will not be sufficient to reach profitability. Furthermore, Nicox cannot guarantee that its choices in terms of cash utilization will prove appropriate. Nicox will need to raise additional funds in amounts that will depend on many factors, including the cost of developing or registering new products and, if appropriate, their commercialization. The Company might therefore have to seek other sources of funding:

- either through capital increases, it being specified that as a result of the volatility of the Nicox share price and constraints imposed in connection with capital increases entailing the cancellation of preferential subscription rights, this source of financing could be considered limited; or

- in the form of a debt; or

- by signing strategic partnership agreements with a view to generate new revenue from patent licenses, or to sharing operating costs with partners;

Nicox cannot guarantee that its future capital requirements will be met or that additional funding will be available on acceptable terms. Turmoil affecting the stock markets has generally made it more difficult to obtain financing by equity securities and could have a materially adverse effect on Nicox's ability to obtain sufficient funding. If the Group were unable to obtain the necessary funding, it could be forced to delay, reduce or eliminate expenses related to certain projects that are under development, to seek funding through partnerships, to grant licenses for the development or marketing of products that the Group would have preferred to develop or market itself, which would have the effect of reducing the added value that the Group might ultimately draw from these products. Such a situation could even jeopardize the continuation of the Company's activities.

2.7.1.2. Specific risks relating to the COVID-19 pandemic which could impact in particular the number of visits to doctors and therefore the amount of sales of VYZULTA and ZERVIATE, the recruitment of patients in clinical trials, and therefore the financial situation of the Company

The sales of VYZULTA and ZERVIATE depend on the number of prescriptions written, which itself depends on the number of visits to doctors. A decrease in the number of visits would result in a decrease in the number of prescriptions and therefore a decrease in revenue for Nicox.

The duration and schedule of the Company's clinical trials depend on the number of patients recruited. If the recruitment is impacted by the COVID-19 pandemic and is no longer in line with the Company's estimates, the trials could take longer than expected and generate additional costs.

The coronavirus pandemic, as well as any other comparable health situation, can have a strong impact on the financial markets, on Nicox's share price, as well as on the Company's ability to finance itself and to advance its development programs on the expected timelines. This could have a significant negative effect on the Company, its business, financial situation and results, as well as on its development and prospects.

There is a risk that the COVID-19 pandemic will disrupt the activities of the Company, its partners and / or subcontractors and therefore have consequences on the development of its product candidates and on its funding needs.

2.7.1.3. Risk related to the Russia / Ukraine conflict

No direct future impacts on the Group's financial situation have been noted following the Russia / Ukraine conflict, which was declared during the month of February 2022. Indeed, to date, the Group has no customers, contractors or suppliers in these territories and did not plan to develop a significant activity there in the short or medium term. The Group also has no direct exposure in terms of research and development. Nevertheless, although this conflict has no significant impact on the performance of the Group, the latter cannot, at this stage, predict the macroeconomic consequences of this geopolitical situation and its evolution, on its future performance.

2.7.1.4. Risks relating to the history of losses and the risk of future losses

To date, the Company has not yet generated significant revenues. The Company has not yet generated profit and has incurred operating losses each year since the commencement of its operations in 1996 which amount to €27.8 million as of December 31, 2022

Almost all the operating losses of the Company resulted from costs incurred in connection with research and development programs and the manufacture of products in preparation for their commercial launch, including activities in clinical and pre-clinical development phases, general and administrative costs linked to the Company's activities.

The payments that Nicox might receive from strategic partners under collaboration agreements might not be sufficient to cover its operating expenses and there is no guarantee, moreover, that the Group will receive additional payments under its collaboration agreements.

Nicox may be expected to continue to incur significant expenses and its operating losses should increase in the near future as a consequence of the significant investments carried out in connection with the development of product candidates.

These operating losses have had and may have a material unfavorable effect on the Company's financial position, cash flows and working capital. For that reason, no assurance can be given that the Company may one day be able to distribute dividends to its shareholders.

2.7.1.5. Risks relating to commitments incurred in connection with bond financing obtained from Kreos Capital

Nicox obtained financing of €20 million from Capital for an amount of €20 million, structured in 3 tranches of secured bonds, the second tranche being divided into two sub-tranches. The first tranche of €8 million was paid on February 1, 2019, the first sub-tranche of €4 million was paid on November 1, 2019, the second sub-tranche of €3 million euros and the last tranche of 5 million euros was called on December 12, 2019 and paid on January 2, 2020. In January 2021 Nicox amended its bond financing agreement with Kreos Capital, introducing an additional one-year period of interest-only payments on the outstanding principal starting on February 1, 2021, and an extension of the overall period of the loan by 6 months to July 2024. This deferral concerns the three tranches of the loan which will therefore be repaid according to the same payment schedule.The new one-year interest-only period was expected to provide approximately €5.5 million of additional flexibility for investment in development activities in 2021.

On November 30, 2021 a new amendment to the bond financing agreement was signed. At that date, the amount of capital still due was €16.9 million, an amount which included €0.6 million prepaid when the tranches were called. These 0.6 million correspond to the last capital payment deadlines for each of the tranches called. Under the terms of the amendment the interest-only period will be increased by 18 months to July 2023 (against January 2022 previously) and the maturity date of the loan increased by 18 months to January 1, 2026. In November 2022, the Company has exercised the option, to further extend the interest-only period and the maturity date by 6 additional months, to respectively January 2024 and July 2026, the Mont Blanc Phase 3 NCX 470 clinical trial having met the primary endpoint of non-inferiority compared to latanoprost before July 1, 2023. This extension will make it possible to defer the repayment of the capital due for the period from August 1, 2023 to January 1, 2024 for an amount of 2.1 million euros. Reimbursement will take place from February 2024 to July 2026. These changes apply to 70% of the outstanding principal, excluding pre-payments of €0.6 million (the “Term Loan”). The interest rateof 9.25% remains unchanged.

In exchange for the extension of the repayment period for an additional 18 months of payment of interest only on the "term loan", €3.3 million of the remaining capital was issued as convertible bonds (the “Convertible Loan”). The term is January 1, 2026 with the same interest rate of 9.25% per annum, payable in cash. The Convertible Loan is secured against the same securities already in place for the Term Loan. This portion of the debt can be converted into shares at Kreos’s discretion at any time (after an initial 60-day period) up to the maturity date of January 1, 2026. The conversion price is €3.67. If Kreos has not converted the Convertible Loan by the end of the repayment period of the Term Loan, the entire amount of the Convertible Loan remaining is due as a single payment at that time. If Kreos converts the Convertible Loan, existing shareholders would be diluted. As with the convertible loan described above, the loan maturity extension option also applies to convertible bonds and will bring their due date to July 1, 2026 instead of January 1, 2026. interest of 9.25% will remain unchanged and interest will be due until maturity on July 1, 2026.

The remaining €1.8 million was issued as a new non-convertible bonds with an interest rate of 9.25%, for the same period as the Convertible Loan and with an additional premium payable at repayment equal to 1.75 times the original amount, including interest. As with the convertible loan and convertible bonds described above, the loan maturity extension option also applies to non-convertible bonds and brings their due date to July 1, 2026 instead of July 1, 2026. January 2026. The interest rate of 9.25% remains unchanged and interest is due until maturity on July 1, 2026.

The interest-only payment period, as well as the option to extend this payment, apply to the Kreos loan as a whole. The option to extend the loan for an additional six months results in an additional interest payment of €0.8 million in 2026.The contract provides for various cases of forfeiture of the term of the loan, in particular the violation of one of Nicox's commitments under a material obligation of the contract could lead to a case such as the payment of the sums due or the failure to transmit financial information; failure to pay a debt of more than €150,000; the initiation of legal proceedings or a cessation of activity. In the event of termination of the term provided for in the contract, the sums due under the loan would become immediately repayable and, in default of payment, Kreos could realize the security. It cannot be guaranteed that Nicox will then have the necessary resources to deal with an early repayment of the loan taken out.

There can also be no assurance that cash flows generated by Nicox will be sufficient to pay the bonds at their maturity which could have a material adverse effect on its business, with security interests having been granted over certain tangible and intangible assets of Nicox S.A., and notably patents relating to the approved product VYZULTA (with the pledge having no impact on the exclusive worldwide license agreement with Bausch + Lomb), securities of the subsidiary Nicox Ophthalmics Inc. as well as a pledge of bank account balances and all receivables of more than €100,000.

2.7.1.6. Risks associated with income and exchange rate fluctuations, reliability of investments

To date the Group’s recurring revenue consist of royalties on sales of VYZULTA and ZERVIATE. The Group considers that there exists an uncertainty about the evolution and stability of this revenue which could potentially impact its sources of funds.

The majority of the Group's expenses are denominated in US dollars

The royalty payments as well as the milestone payments denominated in dollars expected by the Group, in particular through the exclusive worldwide license agreement granted to Bausch + Lomb for VYZULTA, are not significant enough for foreign exchange fluctuations in the value of the euro in relation to the US dollar have a significant impact on the Group's operating results.

The Group does not have significant receivables subject to foreign exchange risks.

The Group also holds US dollar bank accounts that are translated into euros in the consolidated financial statements at each year-end exchange rateand which could be materially impacted by a significant change in the Euro/US Dollar exchange rate. This risk is however mitigated by the fact that cash is exclusively destined to cover the Group's expenses denominated in US dollars resulting from its research and development activities in the United States over the medium term.

2.7.1.7. Market risks

As of December 31, 2022, the Group has no financial instruments and is therefore not exposed to market risk.

2.7.2. Risks relating to products developed by the Company, regulatory authorizations and their commercialization

2.7.2.1. Specific risks relating to NCX 470 and NCX 4251 whose development cannot be guaranteed

NCX 470 is a novel nitric oxide (NO)-donating bimatoprost eyedrop in development for the lowering of IOP in patients with open-angle glaucoma and ocular hypertension. Another Nicox product candidate, which leverages an established molecule, is NCX 4251, a novel patented ophthalmic suspension of fluticasone propionate nanocrystals which is at clinical development stage for dry eye disease.

The first Phase 3 clinical trial, Mont Blanc, necessary for U.S. regulatory approval was initiated in the U.S. in June 2020 following a successful End-of-Phase 2 meeting with the FDA, and the topline results were announced on October 31, 2022. The second Phase 3 clinical trial, Denali, was initiated in November 2020. The Mont Blanc and Denali trials, have been designed to fulfill the regulatory requirements for Phase 3 safety and efficacy trials to support New Drug Application (NDA) filings of NCX 470 in the U.S. and China. The Denali trial is jointly conducted and financed in equal parts by Nicox and our Chinese partner Ocumension and includes clinical sites in both the U.S. and China, with approximately 80% of the patients to be recruited in the U.S. and the remaining 20% of the patients to be recruited in China. Topline results are expected in 2025. This date is based on projections of increased recruitment which take notably into account the lifting of COVID-19 restrictions in China. The management of a multi-country clinical trial is more complex than in one country alone. The Denali trial includes a long-term safety extension with participation of patients from the U.S. and China. On November 7, 2022 the Company announced its intention to seek commercial partnerships for NCX 470 in the U.S. and Japanese markets.

Certain additional clinical and non-clinical data will be required to support NDA submissions. The requirements for a complete Chinese NDA submission may be different from those in the U.S. Changes in the regulatory environment in one country may impact Nicox's products or product candidates in other countries.

The Company has also completed a Phase 2b clinical trial for NCX 4251, Mississippi trial, initiated in December 2020 for the treatment of acute exacerbations of blepharitis, whose results were announced in September 2021. The Mississippi trial did not meet the primary efficacy endpoint of demonstrating complete resolution of the signs (eyelid margin redness and eyelid debris) and symptom (eyelid discomfort) of blepharitis, or secondary efficacy endpoints. However post hoc results suggested that once daily dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, is effective in reducing dry eye symptoms in patients scoring more highly for a key sign of dry eye. . In February 2022 the Company announced that it will be focusing the future development of NCX 4251 on dry eye disease and not in blepharitis as previously considered. Nicox has entirely reviewed its development plan for NCX 4251 as a result of the decision to change the therapeutic indication, which led to an impairment of this asset in the amount of €15,078,000. This impairment was mainly the result of an upward revision of development costs, delays in conducting studies and bringing them to market, and a revision of the percentage of success allocated to future clinical trials. In the first half of 2022, the Company decided to stop the internal development of the product and to seek a partner to develop this product in the U.S., as the development plan for NCX 4251 is not financed. This decision resulted in the recognition of an additional depreciation of 11,029,000 euros, decreasing the net book value of NCX 4251 to zero in the U.S. due to additional costs and timings subsequent to the change of indication, followed by the decision to out-license the product.

The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, providing long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. NCX 4251 is licensed in China to Ocumension Therapeutics. The requirements for a Chinese NDA submission may be different from those in the U.S., and in the event that Ocumension develops NCX 4251 for a different

indication, this may require additional clinical and/or non-clinical data, or further pharmaceutical development. The Company is currently looking for partnerships for NCX 4251 outside of China to advance the development of this program. In the event that the Company does not find a partner to advance the development of NCX 4251 outside of China, and is unable to finance such development itself, there is a risk that the development of NCX 4251 outside of China may be delayed or terminated.

There is a risk that the results of the NCX 470 clinical trials may not be sufficient to move forward with NDA submissions or that additional trials may be necessary to file for approval to commercialize NCX 470.

For NCX 4251, there is a risk that the development required may not lead to a commercially viable business, or that additional trials may be necessary to advance the development or in order to file for approval to commercialize NCX 4251.

Clinical trials or other development activities may be more costly or of longer duration than expected. There is no guarantee that Nicox, or a partner, can file an NDA in the U.S. for NCX 470 or NCX 4251 in the future.

The development of NCX 470 and NCX 4251 could be delayed or fail.

The Company's decisions to find a commercial partner in the U.S. and Japan for NCX 470 and to find a partner to continue the development of NCX 4251 in the U.S. could lead to expected future revenues that are lower than those that the Company could have expected for if these products had been marketed directly, and consequently affect the recoverable value of the goodwill recognized on the balance sheet.

2.7.2.2. Specific risks relating to NCX 470, NCX 4251 and ZERVIATE development in ex-US and ex-China geographies

The Company has multiple collaborations concerning the development and commercialization of its products and product candidates in countries outside of the U.S. and China, and expects to enter into further collaborations in the future. The regulatory requirements in such countries may be different from those in the U.S. and China. If additional clinical or nonclinical studies are required, the Company or its partners may have difficulty finding suitable local contractors.

The development plans for product candidates are currently focused on obtaining regulatory approval in the U.S. initially. For NCX 470, the next expected approval would be in China. Other countries may require additional clinical or non-clinical data to support regulatory approval, which may delay development and launch in those countries. Generating additional data or incorporating the regulatory requirements of those countries into the Company’s development plans may result in delay to, or increase the risk of, the development of such product candidates in those countries.

For products which have been approved in the U.S., the FDA approval may, in some cases, be used as a basis for regulatory approval outside of the U.S. However, there is no guarantee that such regulatory approval will be achieved without generation of additional clinical or non-clinical data, or that the product approved in the U.S. will be approved outside of the U.S.

2.7.2.3. Risks associated with clinical trials and non-clinical studies, affecting mainly NCX 470 and NCX 4251 which could significantly impact the Company's activity in the event of failure or delays

It cannot be guaranteed that the necessary authorizations will be obtained to conduct clinical trials.

There can be no assurance that the authorized trials will be conducted in a timely manner or that they can be conducted without significant additional resources or knowledge. Significant delays in the conduct of clinical trials and non-clinical studies could generate additional costs in connection with the development of the drug

candidates in question. Such delays could also limit the period of exclusivity available to Nicox to commercialize its drug candidates.

Pharmaceutical companies or the regulatory authorities may suspend or terminate clinical trials if they consider that the trial patients are exposed to health risks.

The conduct of clinical trials depends on various factors such as indication, size of the affected population, nature of the clinical protocols followed, proximity between patients and clinical trial sites, eligibility criteria for trials, competition from other companies for the enrollment of patients to conduct clinical trials, availability of sufficient amounts of a compound of appropriate quality, ability to enter into agreements with appropriate subcontractors (and the discharge by them of their contractual obligations), and compliance with the regulatory standards.

The product candidates under development may not have the desired effects or may cause adverse reactions that preclude regulatory approval or limit their marketing potential. It frequently occurs that the favorable results of non-clinical studies and preliminary clinical trials are not confirmed in subsequent clinical trials.

Clinical trials may produce insufficient data to obtain regulatory approval.

This risk concerns mainly NCX 470 and NCX 4251 which are currently under clinical development. The risks related to the development of NCX 470 and NCX 4251 may be different for countries other than the U.S. and China, where development is currently focused.

While VYZULTA and ZERVIATE have been approved in selected territories, they remain subject to risks relating to clinical development in those territories where a marketing authorization is required which remains contingent on the nature of requirements imposed by regulatory authorities in these territories.

2.7.2.4. Risks relating to new products

The development or sale of new products generates risks associated with their novelty.

New Molecular Entities (NMEs) are compounds whose chemical and pharmacological profile is unknown at the time of their discovery. The product candidates under development covered by patents filed by Nicox relating to our nitric oxide (NO) release technology are NMEs. Each NME must be subjected to studies or extensive testing so that its chemical and pharmacological properties can be studied and investigated in detail. The outcome of these studies can entail a degree of uncertainty. Consequently, there can be no assurance that these compounds will demonstrate the same chemical and pharmacological properties in patients as those observed in the preliminary laboratory and animal studies, nor that these compounds will not interact unpredictably and intolerably with human biological functions.

When a molecule achieves first regulatory approval, it may be considered a NME. This classification allows for certain additional periods of marketing or patent exclusivity.

As new compounds, given that the uncertainties of their development, manufacture and properties are not known at the time of their design, difficulties may arise which might cause the company to terminate their development or their sale, thereby potentially affecting the company's prospects or financial position.

Certain product candidates under development by Nicox may include molecules that have already been approved. If the development data relating to the previous development of these molecules is available, Nicox may use it, but there is a risk that a molecule used in another formulation or for another indication or for another route of administration will present new or different side effects. Additional safety studies and/or efficacy studies on the new indication or formulation or route of administration may be required. NCX 4251 is a product candidate containing a molecule which has already been approved.

Recent changes in FDA regulations now consider NCX 4251 and NCX 470 as drug-led combination products in the U.S. This leads to a requirement to generate additional data and the product candidate will be subject to additional review steps for approval in the U.S., which leads to additional costs and or a longer period for the review and approval of NCX 4251 and/or NCX 470 than would have been expected had it been treated purely as a drug product.

2.7.2.5. Risks relating to competition and rapid technological developments

The markets in which Nicox operates are highly competitive and rapidly changing. The Company competes with larger companies with development programs that target the same indications, and with greater experience in the development and marketing of products. In addition, these companies have far greater financial and human resources than the Company. As a result, the Company cannot guarantee that its products:

- Will be able to obtain the required regulatory approval or be brought to market more quickly than those of its competitors;
- Will be able to compete with safer, more effective or less expensive existing or future products, including products which become generic;
- Will adapt quickly enough to new technologies and scientific progress; and
- Will be accepted and selected by medical centers, physicians or patients to replace or complement existing products.

New developments are expected both in the healthcare industry and in public and private research facilities. In addition to the development of safer, more effective and less costly products than those developed or marketed by Nicox, its competitors may manufacture and market products under better conditions. Furthermore, competitors' rapid technology developments, including new products developed during the development of our product candidates, may render Nicox's products obsolete before they can become commercially viable. In certain therapeutic areas targeted by Nicox products and product candidates, such as dry eye and allergic conjunctivitis, products may initially be obtained only by prescription and subsequently sold without prescription, which may have a significant impact on the available market for Nicox products and product candidates.

2.7.2.6. Uncertainty surrounding pricing and reimbursement schemes and reform of health insurance schemes

The ability of Nicox and its partners to secure commercially viable prices for its products that may potentially be marketed in the future depends on several factors, including the profile of its product compared to that of its competitors' products, the price of competing products, the existence of generic products and the targeted geographic area. The Company cannot guarantee that its products will secure pricing agreements for cost-effective marketing within the broader context, where pressure on pricing and reimbursement intensifies (greater control over prices, increased delisting, trend towards the promotion of generics). In some countries, specifically the U.S., the use of Nicox products may be constrained by the need for a patient to try an alternative, generally cheaper, product first before being prescribed a Nicox product. In certain cases, the healthcare prescriber may be required to specifically justify the prescription of the Nicox product in order for the patient to receive reimbursement. Such request can be refused by the company providing the reimbursement.

The commercial success of the Group's products depends in part on the agreement of the regulatory authorities responsible for health insurance, private insurance companies and other similar organizations in terms of product prices and reimbursement rates. Governments and third-party payers seek to control public health expenditure by limiting the reimbursement of new products. The Group cannot guarantee that it, its partners or

its distributors will obtain a high enough reimbursement rate or price for the Company's products and the commercial profitability of these products in the market may consequently be affected.

In addition, pricing and prescribing freedom in some markets are governed and limited by the public authorities. The introduction of more stringent controls on pharmaceutical pricing can have a negative impact on the company's activities, either directly on the products it intends to sell or indirectly on the amount of income that the company can earn through its partnerships and licensing agreements.

2.7.2.7. Risks relating to the market launch of pharmaceutical products

The market launch of pharmaceutical products of the Company is subject to the following risks which could seriously affect the Company's financial position and prospects:

- Regulatory approvals, including approval of branding, may not be granted in time to secure a commercial return;
- The products may be difficult to produce on an industrial scale or their production on an industrial scale may prove too expensive;
- The products may not be profitable because of their cost of production, distribution and/or sale price as imposed by the relevant regulatory authorities;
- The products may not qualify for reimbursement arrangements in some countries, thereby jeopardizing their commercial potential in certain jurisdictions;
- It may be difficult to achieve acceptable quality standards;
- The company may not find a trading partner for the marketing of its products;
- The products may not be marketable on account of rights held by third parties;
- Third parties may market similar products that offer a higher benefit-risk ratio or a more competitive price; and
- A secondary effect or a manufacturing quality problem may arise at any time for a marketed product, which could lead to the restriction or withdrawal of regulatory authorizations for this product.

This risk concerns, in the short term, VYZULTA and ZERVIATE. Specifically, VYZULTA is currently being commercialized by exclusive worldwide partner Bausch + Lomb in more than 15 countries, including the U.S., and is also approved in a number of other countries. However, no assurance can be given that the product will be marketed in other territories. While ZERVIATE has been commercialized in the U.S. by U.S. partner Eyevance Pharmaceuticals (an affiliate of Santen Pharmaceuticals Ltd, Japan) since March 2020, it is possible that ZERVIATE might never be marketed in other territories. With respect to the other product candidates, the risk associated with marketing will persist until a future date in light of their current stage of development.

2.7.2.8. Risks relating to regulatory constraints

The regulatory process may give rise to delays or rejections. The U.S. and European, regulatory authorities tend to impose ever more cumbersome requirements, particularly regarding the volume of data required to demonstrate safety and efficacy. Other regulatory authorities, including China, may also change their requirements for the approval of pharmaceutical products.

Pharmaceutical products cannot be marketed in a given jurisdiction until they have been approved by the relevant regulatory authority, and all pharmaceutical development requires non-clinical and clinical trials to demonstrate the safety and efficacy of the compound under evaluation. The unfavorable outcome of clinical trials or applications for regulatory approval of the therapeutic products developed by the Group is likely to have a material adverse effect on its business.

The achievement of primary endpoints of clinical trials, even with statistically significant results, does not guarantee that the drug-candidate will then be approved by the regulatory authorities. Those authorities may argue that the comparator was inadequate, that the number of patients involved was insufficient, or that the results, although statistically significant, are not clinically significant or that there is inadequate benefit-to-risk to approve the product.

Even after they have been approved, drugs and their manufacturers are subject to continuous and permanent review and the uncovering of problems or the inability to comply with the manufacturing and quality control requirements may lead to restrictions in the distribution, sale or use of these products and even to their withdrawal from the market.

The regulatory authorities have the authority, when approving a product, to impose significant limitations on the product in the form of warnings, precautions and contraindications, or restrictions on the indicated use, conditions for use, labeling, advertising, promotion, marketing, distribution and/or production of the product that could negatively affect its profitability.

The EMA, the U.S. FDA, the Chinese NMPA and similar regulatory bodies may also implement new standards, or change their interpretation and enforcement of existing standards and requirements, for the manufacture, packaging or testing of products at any time. A company that is unable to comply could be subject to regulatory or civil proceedings or be ordered to pay fines.

New regulations may be enacted. Given the disparity of the regulations and procedures, which vary from one country or jurisdiction to another, obtaining authorization in each country within a reasonable time frame cannot be guaranteed.

The Risk Factors addressed here are on the basis of the regulatory environment at the date of this document. Regulatory requirements may be changed by regulatory bodies which may impact either the ability to commercialize already-approved products in the concerned territory, or may increase the costs and the time for development of product candidates. An example is the recent change in the FDA’s position on ophthalmic dispensers, which are now considered medical devices, as noted in section 3.2.4. Specifically. FDA has determined that the language in 21 CFR 200.50(c) indicating that eye cups, eye droppers, and ophthalmic dispensers are regulated as drugs when packaged with other drugs is now obsolete, as these articles meet the 'device' definition.

As part of its research and development work Nicox is, or may be, subject to regulations concerning safety standards, good laboratory practice (GLP), good clinical practice (GCP), current good manufacturing practice (cGMP), the experimental use of animals, the use and destruction of hazardous substances, in addition to regulations and market surveillance good practice (including medical device vigilance and pharmacovigilance) where the products are marketed. In the event of non-compliance with the applicable regulations, the company may be subject to penalties which may take the form of temporary or permanent suspension of operations, withdrawal of the product, restrictions on the marketing of the product and civil and criminal penalties.

2.7.2.9. Specific risks related to VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%

VYZULTA® is a prostaglandin analog with one of its metabolites being NO. VYZULTA was developed for the reduction of IOP in patients with open angle glaucoma or ocular hypertension in the U.S.. The marketing

authorization application for VYZULTA, submitted by its exclusive worldwide licensee, Bausch + Lomb was approved by the U.S. FDA in November 2017. VYZULTA is commercialized in more than 15 countries, including the U.S., and is also approved in a number of other countries.

The Company has identified the main risks related to VYZULTA below. Moreover, it should be noted that all of the "Risks related to Nicox's strategy and business: the research, development and marketing of ophthalmic products" apply to VYZULTA.

Outside of the countries mentioned in the first paragraph, it is still necessary to obtain regulatory approvals before launching VYZULTA on the market. There is no guarantee that Bausch + Lomb will file an application for countries other than these countries, or that if such applications are filed, that they will be successful. There is no guarantee that Bausch + Lomb will launch VYZULTA even after approval has been obtained.

As for marketing authorizations in Europe, a marketing authorization application (MAA) must be filed with the EMA (European Medicines Agency) or – in accordance with the decentralized procedure – with the national regulatory authorities of the European countries covered, which would conduct a validation process and scientific approval to evaluate the safety and efficacy of the drug.

The requirements of the EMA or national regulatory authorities may differ significantly from those of the U.S. FDA and these authorities may request the conduct of different non-clinical and clinical studies.

If VYZULTA has limited or no commercial potential, the Group's activities could be harmed.

Nicox is contractually entitled to receive from Bausch + Lomb net royalties on sales of 6 % to 12 % after deduction of payments owed to Pfizer (see Section 3.2.2.1 for additional information concerning these payments). Royalties received by Nicox depend on sales generated by Bausch + Lomb, which depend on the commercial success of VYZULTA in the countries where it is commercialized and any other territories where it may be commercialized. Nicox cannot guarantee such commercial success. Figures for actual sales may be impacted by the following factors:

- The commercial success of VYZULTA depends on several factors (none of these factors can be guaranteed by the Group), including:
    - Bausch + Lomb's success in obtaining a satisfactory product reimbursement level and sale price after, as applicable, discounts, allowing for viable business development;
    - The maintenance and development of commercial production capabilities at Bausch + Lomb that provide for flexible conditions to ensure enough orders are processed;
    - The continued investment by Bausch + Lomb in medical, marketing and sales support at an appropriate level;
    - VYZULTA's acceptance by the medical community, and, more generally, the success of its launch, commercial sales and distribution.
    - Bausch + Lomb's continued ability to manufacture VYZULTA in accordance with applicable regulatory requirements; and
    - Bausch + Lomb's ability to obtain marketing approvals in other countries for VYZULTA and its wish to apply for such authorizations.

- In addition, restrictions on the use, promotion or sale of VYZULTA or other post-approval restrictions could limit the market potential and reduce the sales volume of the product and its profitability;

Bausch + Lomb has focused its efforts on the United States and countries which accept U.S. FDA approval or reference to existing studies in support of marketing applications in local countries. To our knowledge, marketing applications have not been filed in Europe or Japan and we are not aware of any such plans. In addition, no assurances can be given that such marketing authorizations would be approved. The absence of a marketing authorization for VYZULTA outside of the countries where it is commercialized could limit the commercial success of this product and have a significant effect on the Company's financial position and delay achieving its objectives.

2.7.2.10. Specific risks related to ZERVIATE® (cetirizine ophthalmic solution), 0.24%

ZERVIATE® is an innovative and patented cetirizine-based eye-drop developed to treat ocular itching (itchy eyes) associated with allergic conjunctivitis.

The Company has identified the main specific risks associated with ZERVIATE and has listed them below.

If ZERVIATE has limited or no commercial potential, the Group's activities could be harmed.

In September 2017, Nicox entered into an exclusive license agreement with Eyevance Pharmaceuticals (an affiliate of Santen Pharmaceuticals, Ltd., Japan) for the commercialization of ZERVIATE in the U.S. All manufacturing and regulatory responsibilities, together with decisions on launch timing, lie with Eyevance. Eyevance launched ZERVIATE in a unit-dose presentation in the U.S. in March 2020 and expects a multi-dose presentation in the future. Many countries outside of the U.S. and other major markets base their regulatory approval on FDA approvals. Consequently, the development programs outside of the U.S. may be negatively impacted by the delayed availability of the multi-dose trade unit product presentation and their development risks may increase.

In March 2019, the Company entered into an exclusive license agreement with Ocumension Therapeutics for the development and commercialization of ZERVIATE for a territory comprising mainland China, Hong Kong, Macau and Taiwan or the Chinese market. In March 2020 the license agreement was amended to expand Ocumension exclusive rights to the majority of the Southeastern Asian countries. In February 2022 a Phase 3 clinical trial in China was succesfully completed by Ocumension which has submitted an NDA for the Chinese market in April 2023. The NDA has been included in the priority review and approval process of National Medical Products Administration of the People’s Republic of China (“NMPA”). This will accelerate the approval process and the launch of ZERVIATE expected in China in 2024.

In December 2019, the Company entered into an exclusive license agreement with Samil Pharmaceutical for the development and commercialization of ZERVIATE in South Korea, which was expanded in February 2022 to include Vietnam.

In August 2020, the Company entered into an exclusive license agreement with ITROM Pharmaceutical Group for the development and commercialization in Gulf and Arab markets.

In May 2021, the Company entered into an exclusive license agreement with Laboratorios Grin for the registration and commercialization in Mexico.

No guarantee exists that the Company or its partners will obtain regulatory authorizations to sell ZERVIATE outside the U.S.

The Company does not plan to commercialize ZERVIATE directly in any country and therefore cannot guarantee commercial success. Potential partners make evaluations of the regulatory and commercial

environment concerning products for allergic conjunctivitis, and the potential costs for approving and commercializing ZERVIATE. The Company cannot guarantee that any such evaluations will be positive, and that any positive evaluation will lead to the signature of an agreement.

- Regulatory authorities might impose restrictions on the use or sale of ZERVIATE. These restrictions could limit the potential market, delay the launch and/or reduce the level of sales and profitability of the product.

- The commercial success of ZERVIATE will depend on several factors (none of which can be guaranteed by the Group), including:

    - Availability of the product within the timeframe and in sufficient quantities to support the commercial launch;

    - The maintenance and development of commercial production capacities that provide for flexible conditions to ensure enough orders are processed;

    - In the U.S., Eyevance's success in obtaining a satisfactory reimbursement level and sale price after, as applicable, discounts, allowing for viable business development. This will apply similarly when ZERVIATE is launched in other countries;

    - In the U.S., the continued investment by Eyevance in medical, marketing and sales support at an appropriate level. This will apply similarly when ZERVIATE is launched in other countries;

    - The Company's ability to include new partnerships to develop and market ZERVIATE in other countries;

    - The ability of our partners to obtain regulatory authorizations in other countries; and

    - The acceptance of ZERVIATE by the medical community, and, more generally, the success of the launch, commercial sales and distribution.

    - Eyevance was acquired by Santen Pharmaceutical Co., Ltd of Japan in September 2020. There is a risk this may impact sales of ZERVIATE; and,

    - The US anti-allergy market is changing with many competing products moving from prescription to over-the-counter (without a prescription), and with a significant presence of prescription generics. The impact of these changes led Nicox to revise its estimate of potential future revenues from ZERVIATE in the U.S., resulting in an impairment loss for the U.S. territory of €12,682,000 based on the recoverable amount which is based on the value of usefulness of ZERVIATE. Following this depreciation in value in the U.S, the net book value of ZERVIATE, amounting to 26,000,000 euros, corresponds mainly to the value of the asset assigned to the Chinese territory, for which the rights were granted to the partner Ocumension . In the event of unfavorable circumstances, further write-downs of the residual value of ZERVIATE cannot be ruled out.

2.7.2.11. Product liability and coverage from insurance policies

The use of product candidates under development in clinical trials and the possible sale of drugs may expose the company to liability suits. In the U.S., the approval of a product by the U.S. FDA may only offer limited or indeed no protection against liability claims based on federal state law (federal preemption cannot be invoked),

and the obligations imposed on the company may vary from one federal state to another. If the company cannot successfully defend against liability suits, including liability in connection with clinical trials of its product candidates under development or with future commercial sales of its therapeutic products under development, it could incur heavy liability with potentially adverse consequences for the company.

The insurance policies obtained by the Company might not adequately cover the risks of its existing activities.

Whatever the grounds or eventual outcome of any liability suits, they could result in a fall in demand for a product, a reputation loss for the company, the withdrawal of volunteers from clinical trials, the withdrawal of a product from the market and/or loss of revenue.

2.7.2.12. Environmental and industrial risks, financial risks linked to the effects of climate change

Nicox's research and development activities involve the storage, use and disposal of hazardous radioactive and biological products (see Section 1.2.53 of the Annual Report). Since 2012, these activities have been outsourced. Although these activities are monitored and involve only small amounts of hazardous materials, they pose a risk of contamination to the environment. Even though the Group believes that its activities and procedures comply with standards laid down by applicable laws and regulations, the risk of accidental contamination or injury due to the storage, use and disposal of these hazardous materials cannot be completely eliminated. Nicox could therefore be held liable for amounts over and above the limits of its insurance policy (see Section 2.7.7.1 of the Annual Report). The occurrence of such a risk could have a significant negative impact on the Group's financial position.

The Company has not identified any specific risk, in particular financial, linked to the effects of climate change and has therefore not taken any action in this regard, which does not mean that this risk does not exist.

2.7.3. Risks relating to dependence on third parties

2.7.3.1. Dependence on third parties for carrying out clinical and non-clinical trials

The Company has recourse to subcontractors, and in particular medical institutions, clinical researchers, clinical research organizations to conduct its clinical trials and non-clinical studies. The Company is able to exercise full control over the activity of its subcontractors.

Should its subcontractors fail to respect the terms of their engagement or not succeed in meeting the deadlines provided for within the framework of the trials to be conducted, the Company might be required to delay the development and sale of certain drug candidates.

In the event of default by subcontractors responsible for conducting clinical trials and non-clinical studies, no assurance can be given that the Company will find an alternative solution with other parties which offer acceptable commercial conditions.

In consequence, the occurrence of one or more of these risks could have a material adverse effect on the Group's business, financial position and prospects.

2.7.3.2. Dependence on partners of collaboration agreements and on outside consultants

To maximize its chances of success to launch its products on the market, it could be preferable for Nicox to enter into collaboration agreements with third party companies, and notably Bausch + Lomb for VYZULTA, Eyevance Pharmaceuticals, Samil Pharmaceutical, ITROM Pharmaceutical Group and Laboratorios Grin for ZERVIATE, and Ocumension Therapeutics for ZERVIATE, NCX 4251 and NCX 470.

Company cannot guarantee that it will be able to maintain the collaboration agreements in force, enter into new agreements in future on acceptable terms, or that these agreements will produce the desired results.

When the Company enters into a collaboration agreement, it runs the risk that its partner may unilaterally and arbitrarily terminate the agreement or decide not to market the product. If current partners decided to terminate the agreements in place, or the development of selected compounds, the Company would then have to pursue the development of these products itself, seek new partners or cease their development. Such a situation could increase the company's costs and/or adversely affect its business. The termination or non-renewal of a collaboration agreement could also adversely affect the Company's image and share price.

Conflicts could arise with the company's partners. In addition, the Company's partners could seek to compete with it. The existence of non-competition clauses in the company's collaboration agreements may not provide adequate protection.

Nicox also relies on outside consultants and subcontractors (such as academic researchers, medical specialists, and clinical and pre-clinical research organizations) to develop its products. Agreements between the company and such consultants and subcontractors may include limitation of liability clauses in favor of the other contracting party, in which case the company may not be able to secure full compensation for any losses incurred if the other contracting party fails to perform. Competition for access to these consultants is high, and the company cannot guarantee that it will be able to maintain its existing relationships on commercially acceptable terms. In general, contracting parties may terminate the contract at any time.

The Company depends on the successful execution by its partner licensees of the development plans, regulatory submissions and for obtaining regulatory and marketing approvals for the products. In consequence, the occurrence of one or more of these risks could have a material adverse effect on the Group's business, financial position and prospects.

2.7.3.3. Risks associated with manufacturers, the manufacturing costs of products, the price of raw materials and reliance on third party manufacturers

Because Nicox's products and drug candidates are manufactured by third parties, it has limited control over manufacturing activities. Nicox has neither the infrastructure nor the experience required to manufacture pharmaceutical products. Nicox's dependency vis-à-vis third parties and its lack of experience in commercial-scale production increases the risk of difficulties or delays since its drug candidates are manufactured by third-party manufacturers, for clinical and non-clinical trials, but also for sale after the products have been approved. Unforeseen manufacturing problems could cause delays in commercial sourcing or the clinical trials.

The manufacture of VYZULTA is the responsibility of Bausch + Lomb worldwide.

The manufacture of ZERVIATE for the U.S. is the responsibility of Eyevance. However, in countries whose regulatory approval depends, or will depend, on the U.S. FDA approval of ZERVIATE, any changes in the approval and status of manufacturing may negatively impact Nicox’s development partners and programs in such country. In some cases, a different manufacturer or product presentation may also be required by Nicox’s partners. In such case, transfer of manufacturing may result in delays to regulatory approval.

Nicox might delay the development of its products under development if their manufacture is disrupted, stopped or becomes too expensive. The manufacture of medicines must comply with the applicable regulations and with good manufacturing practices, which is a complex, time-consuming and expensive process. Manufacturers may be subject to inspections prior to approval by regulatory authorities before obtaining marketing authorizations. Even after product approval, the facilities of manufacturers with whom the Company is associated are subject to periodic inspections by regulatory authorities or administrative authorizations that may be suspended. Nicox cannot guarantee that such inspections would not give rise to compliance issues that may prevent or delay marketing authorization, adversely impact the Group's ability to retain approval of the product or its distribution, or oblige the Group to use additional resources, financial or otherwise. Business would be negatively affected should its manufacturers fail to comply with the applicable regulations and recommendations.

2.7.4. Risks relating to the Company's intellectual property

2.7.4.1. Infringement and potential infringement of patents and by other intellectual property rights covering our products and product candidates

The Company, by the nature of its activity, is highly dependent on the protection of its intellectual property.

As far as patent-protected products are concerned, if the patent or patents relating to a product developed, in-licensed or acquired by the company were invalidated or declared unenforceable, the development and marketing of such compound or product would be directly affected or interrupted. The company may, for budgetary or other reasons, not be able to retain its patent portfolio in full, given the high cost of annuities and of potential lawsuits.

Nicox cannot therefore guarantee that:

- It will develop new patentable inventions, or that its patents will allow it to develop commercially profitable products;
- The filed patent applications will be granted;
- If these patents are granted, they will not be challenged, invalidated or declared unenforceable;
- That third parties will not develop products that are not in the scope of protection of its patents; or
- The products that it develops or might in-license or acquire will not infringe, or will not be alleged to infringe, patents or other intellectual property rights owned by third parties.

2.7.4.2. Scope, validity and enforceability of patents

The grant of a patent does not guarantee its validity or its enforceability and may not provide exclusive protection or competitive advantages against competitors with similar products.

To ensure the longest possible exclusivity, the company intends to seek an extension of certain of its patents for a period of up to 5 years. Nevertheless, it cannot guarantee that such extensions will be obtained and failure to obtain these extensions is likely to harm the products concerned. The portfolio of patents and patent applications of the Company covers a number of products. The failure to obtain an extension for patents could have a significant impact for the sale of products concerned and expose the Company to increased competition, which would have consequences on the Company's financial position and prospects.

In particular, the expiration of patents protecting VYZULTA (protection in the U.S. until 2025, which may be subject to extension to 2030), ZERVIATE (protection in the U.S. until 2030 and 2032, in Japan, Canada and Europe until 2030), NCX 470 (worldwide protection under a composition of matter patent until 2029 with potential extensions up to 5 years in the U.S. and EU and formulation patent until 2039 in the U.S., Europe, Japan and China), and NCX 4251 (worldwide protection by patents until 2033 and to 2040 by additional patents granted in the U.S., Europe, Japan and China) could have a material adverse effect on the Company's business and financial position (for additional information, refer to Section 1.2 of the Annual Report).

2.7.4.3. Litigation and defense of patent rights

Competitors can or could infringe the patents of products developed or marketed by Nicox or attempt to circumvent them. The company may have to resort to legal action to enforce its rights, to protect its trade secrets or to determine the scope and validity of others' proprietary rights. Furthermore, the ability of the Group to assert its rights under patents depends on its ability to detect infringements. It is difficult to detect infringers who do not advertise the compounds used in their products.

The protection conferred by a patent in practice varies by product and by country, and depends on many factors such as the nature of the patent, the scope of its protection, the possibility of regulatory extensions, the existence of legal remedies in a given country, and the validity and enforceability of the patents. The laws governing patents are constantly changing and vary from one country to another, with potential for rendering protection uncertain. The Company's patent portfolio includes patents issued in various foreign countries which are on that basis at particular risk.

Any litigation to assert or defend the Group's rights under patents, even if the rights of the Company should prevail, may prove costly in resources and time, and would divert the attention of management teams and key employees from carrying out Company business, which could have a material adverse effect on the Company's operations.

2.7.4.4. Possible infringements of third-party patents

Products developed or in-licensed by the company must not infringe the exclusive rights belonging to third parties. Third parties may also allege infringement by Nicox of their patents or of other intellectual property rights (see Section 3..7.6 "Risks relating to legal and administrative proceedings"). If a legal action is brought against the company on such grounds, there can be no assurance that the company will win the case. Moreover, even if Nicox conducted prior art searches to determine whether its rights infringe the rights held by third parties, it cannot be certain that all relevant rights have been identified because of the uncertainty inherent in this type of search. Such disputes could divert the attention of management teams and key personnel from their task of managing the Company's operations which could have a material adverse effect on the Company's business.

Any claim of patent infringement whose outcome is unfavorable to Nicox could require it to pay significant damages as well as royalties. As a result of claims by third parties, the company may be forced to change or rename its products to avoid infringement of the intellectual property rights of third parties, which could prove either impossible or costly in resources and time. In these circumstances, the Group may have to halt the development and/or sale of these products which may have adverse effects on the Company's financial condition and prospects.

2.7.4.5. Products not protected by intellectual property rights; trade secrets;

The Company may be required in connection with its activities to license or sell therapeutics that are not protected, in all or part of the territories concerned, by intellectual property rights. In this case, it is likely that other market participants will market similar or identical products on the same markets, which may seriously affect the commercial prospects of such products as a result of this increased competition, or indeed the financial condition of the Company.

The development of new therapies by the Company depends in part on protecting trade secrets in order to preserve the confidentiality of technologies and processes used. Where there exists non-public know-how or other trade secrets concerning a product (whether or not the product is patent-protected), the company cannot be certain that confidentiality will be ensured and that such know-how or trade secrets will not be disclosed. If disclosed, the products covered by such trade secrets could see their commercial potential diminished.

2.7.4.6. Risks relating to the protection of trademarks

Nicox is exposed to certain risks related to trademarks. Nicox has submitted applications in numerous countries in order to register several trademarks, particularly for its products. These trademark applications may not result in registration or may be canceled following their registration on the grounds of non-use, revocation or infringement. The company may be denied use of the brand name. Some trademark applications filed by the company may be subject to opposition proceedings. There is no guarantee that the company will be able to resolve these trademark-related disputes and similar disputes in the future. Also, trademarks intended to designate products may be rejected by the relevant regulatory authorities.

2.7.4.7. Employees, consultants and subcontractors

The company cannot guarantee that the confidentiality agreements signed with its employees, consultants and subcontractors will be respected, that it will have adequate remedies for disclosure of confidential information, or that sensitive data will not be brought to the knowledge of third parties in another manner or independently developed by competitors.

Nicox regularly enters into agreements with researchers working in academia or with other public or private entities and, in such cases, the company has entered into intellectual property agreements with these entities. However, the company cannot guarantee that these entities will not claim intellectual property rights over the results of work conducted by their researchers, or that they will grant licenses for such rights to the company on acceptable terms. This would have a significant adverse impact on the company's business and financial condition.

2.7.5. Risks relating to the Company's organization, structure and operations

2.7.5.1. Reliance on qualified personnel

The Company's activities rely on a number of key managers and qualified staff including particularly members of the Executive Committee. Competition for the recruitment of managers and qualified personnel is fierce in the Group's area of activity. The Group's strategy for development and potential expansion requires the continuing expansion of teams by recruiting qualified personnel. The Group cannot guarantee that it will be able to retain the human resources currently available to it or that it will be able to recruit any new resources it might require. The departure of key managers or scientists could delay the achievement of objectives in terms of research and development and the commercialization of products, which would significantly impact the Group's business and prospects.

In addition, the Group's limited workforce does not allow for replacements in the case of the absence of an employee so that the prolonged leave of an employee can significantly disrupt operations.

2.7.5.2. Risks associated with potential future acquisitions of products or companies and with potential future in-licensing transactions

In response to competition and the increasing concentration of resources in the pharmaceutical industry, the Group has carried out and may carry out acquisitions in the future. In addition to the portfolio of assets developed in-house, the Group could acquire rights to product candidates through in-licensing or other transactions, at different stages of advancement. The Group might however be unable to identify appropriate acquisition or licensing targets or conduct acquisitions or licensing transactions under acceptable terms or could even find itself unable to complete the integration of these acquisitions or licensed products, which would be likely to disrupt Group operations and have a negative impact on its activities and its results.

Nicox might continue to seek acquisitions with the aim of optimizing its business model, developing its customer base, accessing new markets and achieving economies of scale. Acquisitions entail certain known and unknown risks that could mean that the Group’s growth and actual operating results differ from its forecasts. Thus, the Group:

- might not manage to identify suitable acquisition targets under acceptable terms;
- might seek acquisitions in foreign countries, which represents greater risks than those inherent to domestic acquisitions;
- might find itself in competition with other companies for acquiring complementary products and activities, which could be reflected by lesser availability or an increase in the acquisition costs of intended targets;

- might not achieve the necessary financing under favorable terms, or not achieve any financing at all, for all or some of the potential acquisitions; or

- the products or activities acquired might not generate results in line with the Group's forecasts, which would then risk not achieving the anticipated revenue and returns.

Furthermore, such an acquisition strategy could divert Management's attention from its existing activities, resulting in a loss of key employees. This strategy could also expose the management to unexpected problems or liabilities, such as successor liability for contingent or undisclosed liabilities related to the activities or assets acquired.

If the Group fails to conduct effective prior assessment of these potential targets (due diligence), it risks, for example,to not identify the problems of target companies or not identify incompatibilities or other obstacles to successful integration. Its inability to integrate future acquisitions satisfactorily could prevent it from receiving all the benefits of these acquisitions and considerably weaken its operational activities. The process of integration may also disrupt its activity and, if new products or activities are not implemented effectively, prevent the Group from fully achieving the expected returns and prejudice its operating results. Furthermore, the total integration of new products or new activities may cause unexpected problems, expenses, liabilities and reactions from the competition. Difficulties related to the integration of an acquisition include the following:

- difficulties in integrating products or activities of the target company with those of the Group;

- incompatibility between marketing and employee management techniques;

- maintaining staff motivation and retaining key employees;

- integrating the cultures of both companies;

- maintaining important strategic customer relationships;

- consolidating corporate and administrative infrastructures and eliminating duplications; and

- coordinating and integrating geographically separate organizations.

Moreover, even if the integration of an acquisition's operations is successful, the Group may not receive all the anticipated benefits, including in terms of the synergies, cost savings and growth opportunities expected. These benefits might not be obtained within the planned deadlines, or even never be obtained, which would have a material adverse effect on the Company's business, financial position, results of operations and prospects.

Furthermore, as a result of acquisitions, the Group may find itself forced to:

- use a substantial portion of its cash resources;

- increase its expenses and its debt level if the Group has to make additional borrowings to finance an acquisition;

- take on liabilities for which the Group is not indemnified by the former owners, given that indemnification obligations may also be the subject of litigation or concerns in connection with the solvency of the previous owners;

- lose existing or potential contracts owing to conflicts of interests;

- suffer adverse tax consequences or deferred compensation charges;

2.7.6. Risks relating to legal and administrative proceedings

Teva Pharmaceutical Industries filed a notice of opposition on November 23, 2016 with the European Patent Office (EPO) against the European patent covering latanoprostene bunod and requested the revocation of the patent as a whole, alleging the absence of novelty or an inventive step. The European patent office rejected this notice of opposition and decided to maintain the patent as delivered. Teva Pharmaceuticals appealed this decision of the EPO on September 12, 2018.

On June 20, 2022, Teva withdrew the appeal and the withdrawal was noted by the Board of Appeal of the European Patent Office on July 7, 2022. Consequently the decision of the European Patent Office has become final and the patent stands as issued. The Group considers that the risk of invalidity of the patent is low, and in consequence has not recorded a provision for this contingency. However, this procedure is by nature uncertain and an unfavorable decision for the Company by this body would have material adverse effects on its business and financial position

The Company contests the application of social security contributions on directors' compensation paid to two non-employee directors whose tax residence is in the United States. By judgment of January 24, 2020, the Court of Justice of Nice approved the claims of the Company; URSSAF appealed this judgment, requesting that it be overturned, the social security charge adjustment confirmed and, as a result, that the Company be ordered to pay €95,054 in principal and €2,000 under Article 700 of the French Code of Civil Procedure. The case was struck from the docket due to the failure of URSSAF to perform procedures. After initiating new procedures, the case was reinstated. The judgement was delivered in favour of Nicox on February 2, 2023, and may still be appealed.

2.7.7. Insurance and risk coverage

2.7.7.1. Insurance

Civil liability of senior officers

The Company purchased a global directors and officers liability policy for Group's senior officers (including directors) including coverage for defense costs before the civil and criminal courts, with a coverage limit for 2022 of €20 million per claim and period of insurance.

General civil liability: Operational, product and professional civil liability

The Company purchased a master policy to cover the civil liability of Nicox Group companies' operations, with a coverage limit for 2022 of €15 million per claim for damage to third parties arising from their operations. The Company obtained an extension of guarantee for Product and Professional Liability in the amount of €15 million per claim and per year of insurance with a deductible of €30,000 per claim. Lower limits of coverage exist for the different guarantees.

This Master Policy provides DIC/DIL (difference in conditions/difference in limits) coverage on top of a local civil liability policy obtained by Nicox Ophthalmics Inc. for the civil liability of the latter within a limit of US$1 million per claim and per insurance year.

Nicox Ophthalmics Inc. took out a compulsory insurance policy to reimburse the wages and medical expenses of employees involved in occupational accidents and diseases (Workers' Compensation) within a limit of US$500,000 and US$100,000 per claim.

Nicox Research Institute purchased coverage for civil liability, civil and criminal legal protection, damage to property, products, its premises, occupational accidents, death and disability for certain designated persons.

Premium for 2022 for the above insurance policies amounted to €250,762,90 including taxes.

2.7.7.2. Risk coverage

Besides the insurance policies described in the preceding section, the Company has taken precautions to ensure continued operations and to avoid any significant loss in the event of a major incident. Computer data is outsourced to a cloud provider and fully outsourced. Daily, weekly and monthly backups are performed on a five-day-rolling basis. Backed up data is stored in a Tier 3 datacenter . The Company entrusts the storage and backup of all materials relating to its clinical studies, its financial data and its human resources data to a specialist company.

2.8. Litigation

There are no administrative, governmental, judicial or arbitration proceedings, including any proceedings of which the Company is aware, whether pending or threatened, that are liable to have, or have had in the last 12 months, a material impact on the financial position or profitability of the Company or the Group other than the proceeding mentioned below.

Disputes with Teva Pharmaceutical

Teva Pharmaceutical Industries filed a notice of opposition on November 23, 2016 with the European Patent Office (EPO) against the European patent covering latanoprostene bunod and requested the revocation of the patent as a whole, alleging the absence of novelty or an inventive step. The European patent office rejected this notice of opposition and decided to maintain the patent as delivered. Teva Pharmaceuticals appealed this decision of the EPO on September 12, 2018. On June 20, 2022, Teva withdrew its appeal and on July 7, 2022, the EPO Board of Appeal closed the appeal proceedings. As a result, the EPO's decision is now final and the patent is maintained as granted.

Dispute with Gland Pharma

In connection with its submission of an abbreviated new drug application (ANDA) to the FDA for approval of a generic version of VYZULTA (latanoprostene bunod), Gland Pharma, an Indian company specializing in generic drugs, is claiming, in accordance with standard practice, that the patents covering VYZULTA are invalid. On June 30, 2022, Bausch + Lomb and Nicox filed a joint complaint against Gland Pharma in New Jersey contesting this allegation (with Bausch + Lomb assuming all costs of this proceeding). As a consequence of this lawsuit, the FDA's regulatory review of the ANDA is automatically suspended for a period of 30 months. Under the terms of the license agreement, Bausch + Lomb will pay all costs related to this proceeding while Nicox will assist Bausch + Lomb in providing all necessary documents and information. This legal proceeding is expected to last for a period of 3 to 4 years. If one or more patents were to be invalidated (within 3 or 4 years), which the Company believes is unlikely, the Company would no longer receive revenue from Bausch + Lomb, it being specified that this would concern revenue generated in the United States.

Dispute with the tax authorities

In February 2019, the Group was informed of a tax audit of the parent company Nicox SA. This audit was completed in September 2020 by a tax deficiency notice concerning €49.6 million in tax loss carryforwards out of a total of €484.6 million available at December 31, 2020 in addition to €0.7 million in withholding tax. The Group strongly contested the merits of these tax adjustments and duly notified the tax authorities by letter on November 10, 2020. In March 2021, the tax authorities withdrew their challenge to a portion of the tax loss carry-forward for €24.8 million. In 2021, after the Group submitted an appeal to a higher authority, the two remaining tax assessments were maintained. In the first half of 2022, a €0.7 million withholding tax was assessed and paid by the Group. The Group filed a claim regarding the assessment of this amount, which was rejected on September 5, 2022. On November 4, 2022, the Company filed an application with the French Administrative Court for relief from the additional withholding tax, including penalties. The Administrative Court acknowledged receipt of this application on November 8, 2022. The Company has not recorded provisions for this dispute. Concerning the second point of the tax adjustment, i.e. the challenge to the tax loss carryforwards arising from the Company's business activities prior to 2016, the Company decided not to bring

the matter before the administrative court and instead corrected its tax loss carryforwards of €24.8 million by reducing their amount in its next tax filing, which should bring an end to the dispute concerning this latter point.

Dispute with URSSAF

The Group contests the application of social security contributions imposed on compensation paid in connection with the offices held by two non-employee directors whose tax residence is in the United States. By judgment of January 24, 2020, the Court of Justice of Nice had approved the claims of the Company. URSSAF appealed this judgment, requesting that it be overturned, the social security charge adjustment confirmed and, as a result, that the Company be ordered to pay €95,054 in principal and €2,000 under Article 700 of the French Code of Civil Procedure. By a decision dated February 2, 2023, which was rendered definitive, the Court of Appeals confirmed the judgment of the lower court, which ruled in favor of the Company's claims.

2.9. Other information contained in the Management Report

2.9.1. Activities

Please refer to Section 1.2 of Part 1 of this Annual Report.

2.9.2. Results

Please refer to the Consolidated Financial Statements, note 3.15 Income tax and the "Consolidated statement of profit or loss".

2.9.3. Five-year financial summary of Nicox SA

Please refer to note 2.27 of the Notes to the Separate Financial Statements.

2.9.4. Risk management

The risks and uncertainties facing the Company are the same as those described for the Group in Section 2.7 of Part 1 of the above management report, as the Company occupies a preponderant position in the scope of consolidation

2.9.5. Dividend policy

The Company has paid no dividends in the previous three fiscal years ended December 31, 2019, 2020 and 2021 respectively.

2.9.6. Disallowed deductions

Pursuant to Articles 223 *quater* and 39.4 of the French Tax Code, the total amount of non-deductible expenses and charges for tax purposes is €13,639,111 and concerns mainly an allowance for impairment of the shares of the US subsidiary.

2.9.7. Existing branch offices

The Group had no branches on the date of this Annual Report.

2.9.8. Loans of less than three years

The Company has not granted any loans to micro-enterprises, SMEs or mid-sized companies.

2.9.9. Statutory disclosures on the AR/AP aged trial balance

Please refer to the table "Statutory disclosures on the AR/AP aged trial balance" in Section 2.1 of this Annual Report.

2.9.10. Shareholder information

Information about the breakdown of the Company's share capital, employee shareholdings and information on transactions carried out by directors and officers during the year ended December 31, 2022 is described in the Corporate Governance Report in Part 2 of this report.

2.9.11. Share buyback program

The Company set up a share buyback program on August 5, 2020 with Kepler Cheuvreux.

The ordinary general meeting of June 28, 2022 authorized the Board of Directors, with the powers to sub-delegate, according to the conditions provided for by articles L. 22-10-62 *et seq*. of the French commercial code, to purchase shares of the Company representing up to 10% of its share capital.

Shares may be acquired pursuant to the decision of the Board of Directors for the following purposes:

- retaining or subsequently tendering shares in payment or exchange, particularly as part of external growth operations;
- implementing stock option plans, restricted share award plans, employee stock ownership plans reserved for participants of a company savings plan, in accordance with the provisions of articles L. 3331-1 *et seq*. of the French labor code, or granting shares to employees and/or executive officers of the Company or companies affiliated therewith;
- tendering shares in the exercise of rights attached to securities giving access to the Company capital;
- canceling all or part of the shares in connection with a capital reduction;
- facilitating orderly trading in the secondary market or the liquidity of the Company share by an investment services provider through a liquidity agreement that complies with an ethics charter recognized by the AMF;
- for use in connection with any hedging operations of the Company's commitments in connection with financial instruments relating notably to changes in the Company's share price; or
- implementing any and all market practices that may be recognized by law or by the AMF.

The acquisition, sale, transfer and exchange of these shares may be carried out, in one or more transactions, by any means, on a market (regulated or otherwise), on a Multilateral Trading Facility (MTF), via a systematic internalizer or over the counter, in particular by the acquisition or sale of blocks of shares, or by recourse to financial derivatives (options, negotiable warrants…) at any time, including in the event of a public offer concerning the Company's shares, in accordance with current legislation. The entire share buyback program may be executed through block trades.

The maximum amount of funds that may be authorized for this share buyback program is €10 million.

This authorization was granted for a period of 18 months as from June 28, 2022.

The implementation of this liquidity contract, pursuant to the authorization granted by the ordinary shareholder meeting of June 28, 2022, will be carried out in accordance with the legal provisions in force and, more specifically, with the provisions of Regulation (EU) No. 596/2014 of the European Parliament and of the Council of April 16, 2014 on market abuse (MAR); the delegated Commission Regulation (EU) 2016/908 of February 26, 2016 supplementing Regulation (EU) No 596/2014 of the European Parliament and of the Council with regulatory technical standards concerning the criteria, procedure and requirements for establishing an accepted market practice and the requirements for maintaining, withdrawing or amending the conditions for

admission; and Articles L. 225-209 et seq. of the French commercial code, and the AMF decision no. 2018-01 of July 2, 2018, applicable as of January 1, 2019.

The following resources were allocated to the liquidity account:

- the sum of €1 million;

The execution of the liquidity agreement may be suspended under the conditions defined in article 5 of AMF decision No. 2018-01 of July 2, 2018.

The execution of the liquidity agreement may also be suspended in the following cases:

- by Nicox, in the event that Kepler Cheuvreux has not made reasonable efforts to meet its obligations with respect to the liquidity of transactions and the regularity of quotations ;
- by Kepler Cheuvreux, when the information provided by the client makes it impossible for Kepler Cheuvreux to meet its obligations;
- by Kepler Cheuvreux, when the sums due to Kepler Cheuvreux under the liquidity contract have not been paid on the payment date, and

The liquidity contract may be terminated subject to the following conditions:

- at any time by Nicox, subject to two (2) business days' notice;
- at any time by Kepler Cheuvreux, subject to a thirty (30) calendar days' notice;
- without notice and without formality if the shares are transferred to another stock market.

Under the liquidity agreement administered by Kepler Cheuvreux on behalf of Nicox, at December 31, 2022 the liquidity account held:

- 288,965 Nicox shares
- €21,815 in cash
- Number of purchase transactions executed in the half-year period: 274
- Number of sale transactions executed in the half-year period: 195
- Trading volume for purchases in the half-year period: 147,703 shares for €249,178
- Trading volume for sales in the half-year period: 100,347 shares for €178,155

At April 27, 2023, 299,367 shares were held under the share buyback program.

Neither the Company nor its subsidiaries hold own shares other than those held under the liquidity program described above.

PART 2 – REPORT ON CORPORATE GOVERNANCE

This report was prepared by the Chairman of the Board of Directors and approved by the Board of Directors on April 28, 2023.

On matters of corporate governance, the Company applies the recommendations of the Middlenext Corporate Governance Code for Small and Midcap Companies" (hereinafter the "Middlenext Code"), available on its website at www.middlenext.com.

3. Corporate governance

3.1. Board composition and practices

3.1.1. Executive Management

At its meeting of May 13, 2022, the Board of Directors decided to separate the functions of Chief Executive Officer of the Company and Chairman of the Board of Directors. As a result, the management of the company is now assured by a Chief Executive Officer. The Chief Executive Officer shall be vested with the broadest powers to act in all circumstances on behalf of the company. The CEO exercises his/her authority within the limits of the Company's purposes and subject to those powers expressly reserved to the shareholders and the Board of Directors and, notably, to the limitations provided for under the Board of Directors' Rules of Procedure.

Biography of the Chief Executive Officer

Andreas Segerros was appointed Chief Executive Officer by the Board of Directors on May 13, 2022, effective June 1, 2022. His term of office is the same as that of the Chairman, as required by law, i.e. until the annual general meeting called to approve the accounts for the year ending December 31, 2023.

Andreas Segerros - Chief Executive Officer - has spent most of his career in global pharma, with executive positions (R&D, Marketing and Business Development) in the U.S., Europe and Japan, at Pharmacia, Pharmacia & Upjohn and Ferring, with the focus on specialty Pharma, ophthalmology in particular. As Global Head of Ophthalmology at Pharmacia, Andreas launched XALATAN® (latanoprost), making it the industry's first billion-dollar ophthalmic drug. His venture capital experience comes from being Partner at the Scandinavian group Sunstone Capital, and also co-founded Eir Ventures. Andreas has made numerous investments in successful companies in Europe and the U.S. Andreas holds an MSc in Organic Chemistry from the Royal Institute of Technology in Stockholm, Sweden, and an MBA in International Financing from the University of Uppsala, Sweden.

Michele Garufi served as Chairman and Chief Executive Officer until May 31, 2022, when the Board of Directors terminated his duties.

3.1.2. Membership of the Board of Directors

Nicox SA is governed by a Board of Directors with 6 members, all of whom are considered independent in accordance with the criteria set out in the MiddleNext Code, and whereby the Chief Executive Officer is not a director. The Company is committed to the principle of equal representation of men and women. Two of the Board of Directors' six members are women.

Five directors are members of special committees:

- Audit Committee: Jean-François Labbé (Chair), Luzi Von Bidder, Lauren Silvernail
- Compensation Committee: Adrienne Graves (Chair), Jean-François Labbé, Lauren Silvernail
- Corporate Governance Committee: Lauren Silvernail (Chair), Luzi von Bidder, Les Kaplan

- Science and Technology Committee: Les Kaplan (Chair), Adrienne Graves
- Corporate Social Responsibility Committee: Lauren Silvernail (Chair), Luzi von Bidder, Les Kaplan

Biographies of the Directors

Jean-François Labbé has been Chairman of the Board of Directors of Nicox since July 2022, a Director of Nicox since June 2010, Chairman of the Audit Committee since July 2013 and a member of the Compensation Committee. His term will expire at the end of the annual general meeting called to approve the financial statements for the year ended December 31, 2023. His membership to the Board was proposed by the Banque Publique d'Investissement in 2010. Mr. Labbé is the Founder and Chief Executive Officer of SpePharm Holding BV, a pan-European specialty pharma company. Prior to founding SpePharm, M. Labbé served as Chief Executive Officer of OTL Pharma SA from 2001 to 2004 and as chief operating officer of ProStrakan UK from 2004 to 2005. He has spent his career in the pharmaceutical industry first at Roussel Uclaf in 1974, then Hoechst Roussel and HMR, where he served in various positions in Europe, the United States and was a member of the HMR's Executive Committee before its merger with Aventis in 1999. Mr. Labbé holds an MBA from the Ecole des Hautes Études Commerciales (HEC), Paris (France). Mr. Labbé is 73. He can be contacted at 27 allée des Bocages, 78110 Le Vésinet (France). He does not hold any Nicox shares.

Michele Garufi has been a director since February 15, 1996. His term as director will expire at the end of the annual general meeting called to approve the financial statements for the year ended December 31, 2024. He was Chairman and Chief Executive Officer of the Company until May 2022 and Interim Chairman in June and July 2022. Michele Garufi was born in Milan, Italy in 1954 and graduated with honors with a degree in pharmaceutical chemistry from the University of Milan in 1977. Mr. Garufi earned a pharmacist's degree in 1989 from the University of Padua. Michele Garufi has extensive experience in partnerships management, licensing agreements and international marketing in the European pharmaceutical industry. Before 1996, he served as Vice President of the International Division and Director of Licensing Activity at Recordati Italy and as CEO of the Spanish subsidiary of Recordati Italy from March 1992 to March 9096. Prior to those positions, he was the Director of the International Division of Italfarmaco (1988-1992), assistant to the Chief Executive Officer of Poli Chimica (1984-1988), assistant to the President of Yason Research (1983) and Technical Director for one of the Italian subsidiaries of the French group Lipha (1978-1982). Michele Garufi is currently co-founder and member of the Board of Directors of LaMed Pharma Srl, co-founder and member of the Board of Directors of NanoRetinal Inc, co-founder and member of the Board of Directors of Golgenia Srl. He is also an advisor to the Italian venture capital fund BIO Indaco. M. Garufi is 69. In his youth, he was a member of the National Italian Swimming Team. He may be contacted at the following address: Via Torquato Tasso 10, 20123 Milan, Italy. On the date of this report, he held 592,051 shares.

Adrienne L. Graves, Ph.D. was coopted to the Board of Directors of Nicox in August 2014. She is Chair of the Science and Technology Committee. His term will expire at the end of the annual general meeting called to approve the financial statements for the year ended December 31, 2024. Dr. Graves is a visual scientist by training and a global industry leader in ophthalmology. She served as president and chief executive officer of Santen Inc., the U.S. subsidiary of Santen Pharmaceutical Co., Ltd., from 1995 to 2010, where she successfully established a strong global presence and led global teams through successful acquisitions and partnerships. Prior to her fifteen years at Santen, she spent nine years at Alcon Laboratories, Inc., where she joined as Sr. Scientist to establish Alcon's first Visual Function Laboratory and progressed through roles of increasing responsibility in R&D, including directing clinical development in multiple therapeutic areas and serving as Director of International Ophthalmology. Dr. Graves currently is Chair of IVERIC bio, an American corporation, and serves as an independent director on the boards of Greenbook TMS, a Canadian corporation, Qlaris Bio, TherOptix and Surface Pharmaceuticals (U.S private companies). Dr. Graves also serves on the boards of the American Society of Cataract Refractive Surgery Foundation (ASCRS) in the United States, the Glaucoma Research Foundation in the United States, Retina Global, Himalayan Cataract Project, a U.S. foundation, and

the Foundation Fighting Blindness in the United States and as a director emeritus of the American Academy of Ophthalmology Foundation. She previously served on the boards of Encore Vision (2011-2017, acquired by Novartis), Envisia Therapeutics (2014-2017, acquired by Aerie Pharmaceuticals), TearLab Corporation (2005-2018), Akorn (2012-2020), Aerpio Therapeutics (2012-2017) and Oxurion NV (2019-2023). She co-founded OWL (Ophthalmic World Leaders) and Glaucoma 360. Dr. Graves received her AB with honors in psychology from Brown University and her Ph.D. in psychobiology from the University of Michigan. She completed a postdoctoral fellowship in visual neuroscience at the University of Paris, France. She is 69. Ms. Graves can be contacted at 401 Harrison Street #34E, San Francisco, CA 94105, USA. She does not hold any Nicox shares.

Luzi A. von Bidder was coopted to the Board of Directors of Nicox in August 2014. He is a member of the Audit Committee, the Corporate Governance Committee and the Corporate Social Responsibility Committee. His term will expire at the end of the annual general meeting called to approve the financial statements for the year ended December 31, 2024. He was the Chair of Acino Holding AG until 2013. Mr. Von Bidder was the Chairman-CEO of Novartis Ophthalmics AG. He has also served as a member of the Novartis Pharma Executive Committee and served in various positions at Ciba Geigy Corp. Mr. von Bidder is a member of the board of directors of Ferring Pharmaceuticals, Ferring Ventures, Ixodes AG, Oculocare, Orasis and EyeSense GmbH, where is also the Chairman of the Board of Directors. Mr. von Bidder graduated in Economics from HSG University of St. Gallen (Switzerland). He is 70. He may be contacted at Kirchenweg 5, 8008, Zürich, Switzerland. He holds 10,000 Nicox shares.

Les Kaplan has been a Nicox director since October 2014. He is Chair of the Science and Technology Committee, and a member of the Corporate Governance Committee and the Corporate Social Responsibility Committee. His term will expire at the end of the annual general meeting called to approve the financial statements for the year ended December 31, 2025. A proposal has been submitted to the Ordinary General Meeting to be held on June 14, 2022 for the renewal of his term for four years. He was the Executive Chairman of Aciex Therapeutics, Inc., a pharmaceutical development company acquired by Nicox in October 2014. Dr. Kaplan began his career at Allergan Inc., where he served as president, research and development and led approvals of over 20 major pharmaceutical products and indications. Prior to joining Allergan, Dr. Kaplan held research positions at the Upjohn Company and at the University of California, Los Angeles, and instructed in chemistry at both Temple University (Philadelphia) and UCLA. He previously has served on the boards of Allergan, Altheos (USA), Acadia Pharmaceuticals, Inc (USA) and Neurotech, Inc (USA). Dr. Kaplan received a B.S. in chemistry from the University of Illinois (USA), and a Ph.D. in organic chemistry from the University of California, Los Angeles (USA). He is 71. He can be contacted at 1710 Anglers Drive, Steamboat Springs, CO80487, United States. He holds 82,034 Nicox shares.

Lauren Silvernail was appointed director of Nicox in May 2017. She is the Chair of the Corporate Governance Committee and the Corporate Social Responsibility Committee and a member of the Audit Committee and the Compensation Committee. Her term will expire at the end of the annual general meeting called to approve the financial statements for the year ended December 31, 2024. She is also currently Chair of the Audit Committee and a member of the Board of Directors of Harpoon Therapeutics. From 2018 to 2022, Ms. Silvernail is Chief Financial Officer and Executive Vice President, Corporate Development of Evolus, Inc. Before joining Evolus, from 2013 to 2018 Ms. Silvernail was Chief Financial Officer and Chief Business Officer of Revance Therapeutics Inc. Before joining Revance, Ms. Silvernail was Chief Financial Officer and Vice President, Corporate Development of ISTA Pharmaceuticals, Inc. from 2003 to 2012. Between 1995 and 2003, Ms. Silvernail served in different operational and corporate development roles for Allergan Inc., including Vice President of Business Development. From 1990 to 1994, she was a general partner of Glenwood Ventures and a member of the boards of directors of several Glenwood portfolio companies. Ms. Silvernail began her career at Varian and Bio Rad Laboratories. Ms. Silvernail received a B.A. in biophysics from the University of California, Berkeley, and an M.B.A. from the University of California, Los Angeles. She is 63. She may be contacted at 10 Hertford, CA 92657 Newport Coast, United States. She does not hold any Nicox shares.

Independence of the directors

To the Company's knowledge, there are currently no contractual or family ties among the corporate officers of the Company.

The internal rules of the Board of Directors, which were updated in 2022 following the decision to refer to the MiddleNext Corporate Governance Code, stipulate that the Board must have, to the extent possible, two directors considered to be independent, and that it must reevaluate the independence of its members under the criteria set by the Board every year.

The Board decided that the criteria for evaluating the independence of Board members would be the criteria defined in the Middlenext Code as updated in September 2021, i.e.:

- they must not have been during the last five years an employee or executive officer of the company or a company in its group;
- they must not have had any material business relationship with the company or its group for the last two years (as a client, supplier, competitor, service provider, creditor, banker, etc.);
- they must not be a reference shareholder of the company or hold a significant percentage of voting rights;
- the member has no close family ties with a corporate officer or a reference shareholder;
- they must not have been an auditor of the company in the course of the previous six years.

At its meeting of December 16, 2022, the Board considered that under the above-mentioned criteria of the Middlenext Code all directors should be considered independent.

Moreover, the Board of Directors' internal rules of procedure require each director to provide, before the end of each fiscal year, a statement describing his/her relationship with the Company, the members of the Board of Directors and its Chief Executive Officers and a declaration on the existence of possible conflicts of interest.

In declarations made at the end of 2022, the six directors declared that they were not related, directly or indirectly, to any of the Group's companies, nor to their directors or chief executive officers.

As provided for in the Board of Directors' internal rules of procedure, directors having a conflict of interest must inform the Board, abstain from voting or taking part in its deliberations and, if necessary, resign. The absence of any information to this effect will be deemed to be acknowledgment that no such conflict of interest exists.

Directors

The Company is administered by a board of directors. The number of directors shall not be less than three and not more than eighteen. However, in the case of a merger, the Board of Directors may include and maximum of twenty-four members for a period of three years from the date of the merger as set by article L.236-4 of the French commercial code.

Directors are appointed by the Ordinary General Meeting of the shareholders. Directors may be co-opted under the conditions provided for by law.

Their terms of office as directors is for four years.

The term of office of directors ends at the end of the Annual General Meeting called to approve the financial statements for the previous year, which is held in the year in which the term expires.

The age limit to serve on the Board is 79. A director who reaches the age limit shall be considered to have automatically resigned as of the date of the next ordinary general meeting, which will note this resignation.

Subject to this reservation, directors may always be re-elected.

The Board of Directors carries out the inspections and verifications it deems necessary. The Chairman or the Chief Executive Officer of the company shall ensure that each director is provided with all documents and information necessary for the performance of his or her duties.

Non-voting Advisors

The ordinary general meeting may also appoint one or more persons with the title of non-voting advisor for a term of four years. The non-voting advisors attend the meetings of the Board of Directors, but have no voting rights on the decisions submitted to the Board. The non-voting advisors are called to Board meetings under the same conditions as the directors, and have the same rights to information.

There are presently no Non-voting Advisors with the Company.

Service contracts

There are no service contracts binding the members of the administrative or management bodies to the Company, or to any of its subsidiaries, which stipulate advantages under the terms of such contracts.

3.1.3. Other offices

The following table provides a summary of all the current offices and positions held in any company by each of the directors in 2022 as well as any other offices held during the last five years.

Corporate offices	Offices within the company			Offices and positions held outside the group on the filing date of the annual report					
Last name, first name and date of birth	**Date of first appointment**	**Expiration date of current term**	**Principal position held in the Company**	**Positions held**	**Name or corporate name**	**Legal form**	**Country of registered office**	**Offices and positions outside the group held during the last five years having expired**	**Nicox shares held in treasury at 12/31/2022**
Labbé Jean-François 03/15/1950	06/16/2010	Shareholders' meeting called to approve the financial statements for the year ending 12/31/2023	Independent director	Director*	Deinove	SA	France	Director of Transgène SA France until June 2018	0
			Chairman of the Board of Directors since July 28, 2022	Managing Director	SpePharm Holding	BV	Netherlands	Director of Algotherapeutix (France) until September 2020	
			Chairman of the Audit Committee	Managing Partner	Arcade	SARL	France		
			Compensation Committee member						

* until February 2022

Corporate offices	Offices within the company				Offices and positions held outside the group on the filing date of the annual report					
Last name, first name and date of birth	**Date of first appointment**	**Expiration date of current term**	**Principal position held in the Company**	**Independent**	**Positions held**	**Name or corporate name**	**Legal form**	**Country of registered office**	**Offices and positions outside the group held during the last five years having expired**	**Nicox shares held in treasury at 12/31/2022**
Garufi Michele 02/03/1954	02/15/1996	Shareholders' meeting called to approve the financial statements for the year ending 12/31/2024	Director (Chairman-CEO until May 31, 2022, Interim Chairman in June and July 2022)	No	Director	LaMed Pharma	Srl	Italy	Director of Eagleye Biosciences (Switzerland)	592,051
					Director	NanoRetinal	Inc.	United States		

Corporate offices	Offices within the company			Offices and positions held outside the group on the filing date of the annual report					
Last name, first name and date of birth	**Date of first appointment**	**Expiration date of current term**	**Principal position held in the Company**	**Positions held**	**Name or corporate name**	**Legal form**	**Country of registered office**	**Offices and positions outside the group held during the last five years having expired**	**Nicox shares held in treasury at 12/31/2022**
von Bidder Luzi Andreas 04/09/1953	08/11/2014	Shareholders' meeting called to approve the financial statements for the year ending 12/31/2024	Independent director	Chairman of the Board of Directors	EyeSense	AG	Switzerland	Solvias AG (Switzerland)	10,000
			Audit Committee member	Director	Ferring	SA	Switzerland	Ocular AG (Switzerland)	
			Corporate Governance Committee member	Director	Ixodes	AG	Switzerland		
				Director	Orasis	Limited	Israel		
			Corporate Social Responsibility Committee member	Director	Ferring Venture	SA	Switzerland		

Corporate offices	Offices within the company			Offices and positions held outside the group on the filing date of the annual report					
Last name, first name and date of birth	**Date of first appointment**	**Expiration date of current term**	**Principal position held in the Company**	**Positions held**	**Name or corporate name**	**Legal form**	**Country of registered office**	**Offices and positions outside the group held during the last five years having expired**	**Nicox shares held in treasury at 12/31/2022**
Kaplan Les 08/06/1950	10/22/2014	Shareholders' meeting called to approve the financial statements for the year ending 12/31/2025	Independent Director					Director of Acadia Pharmaceuticals, Inc. (USA)	82,034
			Chair of the Science and Technology Committee					Chair of the Board of Directors of Aciex Therapeutics, Inc. (United States)	
			Corporate Governance Committee member					Director of Neurotech, Inc. (USA)	
			Corporate Social Responsibility Committee member						

Corporate offices	Offices within the company			Offices and positions held outside the group on the filing date of the annual report					
Last name, first name and date of birth	**Date of first appointment**	**Expiration date of current term**	**Principal position held in the Company**	**Positions held**	**Name or corporate name**	**Legal form**	**Country of registered office**	**Offices and positions outside the group held during the last five years having expired**	**Nicox shares held in treasury at 12/31/2022**
Graves Adrienne 12/14/1953	08/08/2014	Shareholders' meeting called to approve the financial statements for the year ending 12/31/2024	Independent director	Director	Retina Global	Foundation	United States	Director of Envisia Inc. (United States)	0
			Chair of the Compensation Committee	Director	Qlaris Bio	Inc.	United States	Director of Aerpio Therapeutics Inc. (United States)	
			Science and Technology Committee member	Director	TherOptix	Inc.	United States	TearLab Inc (United States)	
				Director	Foundation Fighting Blindness	Foundation	United States	Director of Encore Vision Inc. (United States)	
				Director	Surface Ophthalmics	Inc.	United States	Director of Akorn Inc. (United States) until September 2020	
				Director	Oxurion	NV	Belgium		
				Director	Greenbrook TMS		Canada		
				Chairman of the Board of Directors	Iveric Bio		United States		
				Director	Glaucoma Research Foundation	Foundation	United States		
				Director	ASCRS Foundation	Foundation	United States		
				Director	Himalayan Cataract Project	Foundation	United States		
				Director Emeritus	American Academy of Ophthalmology Foundation	Foundation	United States		
				Director	Opus Genetics	Inc.	United States		

Corporate offices	Offices within the company			Offices and positions held outside the group on the filing date of the annual report					
Last name, first name and date of birth	**Date of first appointment**	**Expiration date of current term**	**Principal position held in the Company**	**Positions held**	**Name or corporate name**	**Legal form**	**Country of registered office**	**Offices and positions outside the group held during the last five years having expired**	**Nicox shares held in treasury at 12/31/2022**
Silvernail Lauren 09/07/1958	05/16/2017	Shareholders' meeting called to approve the financial statements for the year ending 12/31/2024	Independent director	Chief Financial Officer	Harpoon, Inc NASDAQ: HARP	Corporation	United States	Evolus, CFO and EVP of Corporate Development	0
			Compensation Committee member					Revance Therapeutics, CFO and Chief Business Officer	
			Audit Committee member						
			Chair of the Corporate Governance Committee						
			Chair of the Corporate Social Responsibility Committee						

3.1.4. Conditions for the preparation and organization of the work of the Board of Directors

Internal rules of the Board of Directors

The operation of the Company's Board of Directors and its working committees is governed by rules of procedure that were updated in 2022, primarily to establish a new working committee, namely the Science and Technology Committee.

These internal rules contain provisions on the following:

- The powers of the Board of Directors. The internal rules stipulate that the Board defines the strategies of the Company's activities and ensures that they are implemented. Subject to the powers expressly granted to shareholders' meetings, and within the limits of the corporate purpose, the Board considers any question that is relevant to the proper operation of the Company and decides the Company's affairs through its resolutions. In particular, the Board rules on the budget, the business plan and, in general, any major transaction. In the event of a difference between a decision of the Board and a MiddleNext recommendation, the Board shall provide an explanation for this difference (according to the "*comply or explain* " principle).

- The composition of the Board of Directors, in order to ensure and monitor its independence. Thus, the internal rules stipulate that the Company's Board must have, to the extent possible, at least two independent members. The independence of the directors must be reevaluated annually by the Board on the basis of the criteria set forth in the revised MiddleNext code of September 2021.

- The procedures and conditions for meetings of the Board of Directors. The Internal Rules of Procedure stipulate that, subject to the limits and exceptions provided by law, directors who participate in the meeting via videoconferencing or electronic methods that allow identification and guarantee effective participation, the nature and conditions of which shall be defined by the regulations in force and subject to reservations stipulated by said regulations, shall be deemed present for calculating the quorum and majority. In this respect, it is specified that participation via videoconferencing or electronic methods is not open for Board meetings called for the purpose of establishing the annual financial statements, the consolidated financial statements and the management report.

- The procedures for information to the members of the Board of Directors. In particular, the Internal Rules of Procedure provide for an obligation to regularly inform the directors of the Company's financial position, about the cash it holds and its financial commitments. It also provides that the Chairman of the Board of Directors must provide Board members with all significant information concerning the company. The internal rules stipulate, for each member of the Board, the right to obtain any information or document the member believes he needs to perform his duties and/or to meet with any of the senior executives of the company outside the presence of the Chair of the Board. The rules also provide that directors must receive, prior to meetings, all documents and information required for them to perform their mission. These documents and information shall be transmitted to them by email to the extent possible, approximately one week before the meeting.

- The list of the decisions for which the Chief Executive Officer must obtain prior approval from the Board. This list includes: decisions to establish operations in international markets or withdraw from foreign sites; significant transactions that could impact the Group's strategy or modify its financial structure or scope of activity; the acquisition or sale of stakes in other companies; all transactions covering assets, securities or stocks; the acquisition or sale of real estate; the granting of sureties on corporate assets, or obtaining loans in excess of €150,000.

- The conditions for appointment and the role of the Working Committees. The internal rules stipulate that the Board may form committees to prepare its work. The Board defines the role assigned to each committee; it is specified that these committees operate under the exclusive and collective responsibility of the Board members. The mission of the committees is to clarify the Board's decisions through their analyses, and they formulate proposals, recommendations and opinions for this purpose. The members of the committees must personally participate in the meetings and may not be represented by another member. The committees may not deliberate with fewer than half the members. The committees can consider any question falling within their area of expertise. They may also be petitioned by the Board of Directors or the Chair.

- Audit Committee responsibilities. The mission of the Audit Committee is to ensure the quality of the Internal Audit and the reliability of the information provided to shareholders and the financial markets. In particular, it is responsible for monitoring the process to prepare the financial information, evaluating procedures, monitoring the control of the parent company and consolidated financial statements by the Statutory Auditors (review of the assumptions used to close the financial statements, review of the annual, half-yearly and quarterly financial statements, if applicable, before they are reviewed by the Board of Directors, a review, in consultation with the Statutory Auditors, of the accounting principles and methods used, examination of the major transactions that might generate a conflict of interest), monitoring the independence of the Statutory Auditors, the procedure for selecting them, their fees, and the use of the Statutory Auditors for work other than auditing the financial statements.

- Audit Committee members. The Audit Committee is comprised of three members, all independent directors appointed for the duration of their term as board members that includes at least one member with specific expertise in finance or accounting. The Chairman-CEO is not a member of the Audit Committee. The Audit Committee meets whenever it deems necessary and at least twice a year before the Board meetings that review the annual and half-yearly financial statements. The Audit Committee may conduct visits or audition managers of operating or functional entities that are useful for performing its mission. It may also meet with the statutory auditors, including outside the presence of the senior executives. It may be assisted by outside experts subject to the Board of Directors' authorization

- Compensation Committee responsibilities. The mission of the Compensation Committee is to make recommendations on the general compensation policy for executive corporate officers (fixed and performance-based, in-kind benefits, retirement, severance packages), and the award of restricted stock units (*actions gratuites*), stock options or equity warrants; to make recommendations concerning all elements of compensation for each executive officer (including in-kind benefits); to make proposals concerning the total allocation for directors' compensation and its allocation, on all elements of compensation (including the award of stock options or free shares) and for the principal executives (Senior Managers, Vice Presidents, Vice President for Finance); to review the annual increase in the payroll; to review plans to grant shares and stock options, and the criteria and conditions applicable to these grants; to collect information about the compensation and benefits paid to the corporate officers of the Company and the companies that it controls.

- Compensation Committee members. The Compensation Committee has three to five members, half of whom should be considered independent, if possible. The Chief Executive Officer is not, in principle, a member of the Compensation Committee. The Compensation Committee meets whenever it deems necessary, and at least once a year. The Compensation Committee may ask the Chair to provide any document or interview any person.

- The responsibilities of the Corporate Governance Committee. The mission of the Corporate Governance Committee is to propose criteria to evaluate the independence of Board members, assess the effectiveness, relevance and implementation of the corporate government procedures, and to make recommendations to improve them, submit proposals on the composition and responsibilities of the committees, and examine candidates for director and strategic management positions.

- The members of the Corporate Governance Committee. The Corporate Governance Committee has three to five members, half of whom are considered independent, if possible. The Chief Executive Officer is not, in principle a member of the Corporate Governance Committee, but he participates in the work of the Committee to select directors and corporate executive officers. The Corporate Governance Committee meets whenever it deems necessary, and at least once a year. The Corporate Governance Committee may ask the Chair to provide it with any document or interview any person.

- Science and Technology Committee responsibilities. The mission of the Science and Technology Committee is to assist the Board in supervising the scientific and technical aspects of the company's activities and periodically provide the Board with information. Its mission consists mainly in assisting the Board in supervising the objectives of the R&D programs by examining progress and performances of management in meeting the objectives and by limiting the associated risks, examining the Company's research pipeline, examining recommendations of the Board on the scientific, technical and medical aspects of operations which must be submitted to the Board for approval, identifying new trends and significant developments in the area of science and R&D and their potential impact on the Company, reviewing the Company's intellectual property portfolio and its strategy in

this area, performing all activities that the Committee shall deem necessary or appropriate to exercise its responsibilities to assist the Board in supervising the Company's R&D activities. The Committee may, in connection with its missions, request the Chairman to provide it with any document or allow it to meet with any person, and notably the Chief Scientific Officer, the Head of Development, the Chief Business Officer, the Chief Financial Officer and external advisors.

- Composition of the Science and Technology Committee. The Committee is comprised of at least two and not more than five directors. To the possible, the members shall be considered as independent. In principle, the Chairman of the Board of Directors, the Chief Executive Officer and the Executive Vice President are not members of the Science and Technology Committee. However, the Chairman of the Board of Directors is associated with the work of the Committee at the request of its members. The Committee meets whenever it deems necessary, and at least three times a year. It sets the calendar of its meetings. It may also meet at the request of two of its members, its Chair or the Chairman of the Board of Directors.

- Corporate Social Responsibility Committee responsibilities. The Committee assists the Board in overseeing the social, societal and environmental aspects of the Company's activities and regularly provides information to the Board. Its mission is to examine employment, social and environmental issues and to consider areas for improvement to be proposed to the Board, in particular to help the Board consider how to share value and achieve a balance between the level of employee compensation, compensation for shareholder risk-taking and the investments needed to ensure the company's long-term sustainability. The CSR Committee works in coordination with other committees, according to the issues involved.

- Corporate Social Responsibility Committee members. The Committee is comprised of at least two and not more than five directors. As far as possible, it is composed of members considered to be independent, and is chaired by an independent member. In principle, the Chairman of the Board of Directors, the Chief Executive Officer and the Executive Vice President are not members of the CSR Committee. However, the Chairman of the Board of Directors is associated with the work of the Committee at the request of its members. The Committee meets whenever it deems necessary, and at least once a year. It sets the calendar of its meetings. It may also meet at the request of two of its members, its Chair or the Chairman of the Board of Directors. The Committee may, as part of its mission, ask the Chairman to provide it with all documentation or allow it to consult with any person, including external advisors. It may be assisted by qualified persons, as needed.

- Principles for allocating directors' compensation. For the distribution of directors' compensation, the Board may take into consideration the activity of the directors, attendance of members at Board meetings, and any participation in the work of the Committees.

- A restatement of the confidentiality obligations;

- A restatement of the legal obligation for members of the Board of Directors to hold their shares in registered form;

- The declaration procedures for transactions executed by the directors and their relatives in securities of the Company, which stipulates an obligation for Board members and chief executive officers to declare in writing each of the transactions they, or their families, have executed in securities of the Company to the French *Autorité des Marchés Financiers*, within five trading days, in accordance with the procedures and force;

- Recommendations to prevent insider trading.

In addition, the Board of Directors adopted, for its employees and officers, recommendations to prevent insider trading in the Company. These recommendations contain a list of precautions to take to preserve the confidentiality of sensitive information; a general obligation to abstain if privileged information is held, and a specific obligation to refrain from executing any transaction in Nicox financial instruments (or financial instruments related to Nicox securities) for thirty calendar days before, and one day after, the publication of the annual and interim results and fifteen calendar days before, and one day after, the publication of quarterly financial information.

Provisions of the By-laws

The Company is administered by a Board of Directors currently composed of six members.

Their terms of office as directors are for four years. The term of office of directors ends at the end of the ordinary general meeting called to approve the financial statements for the past year, which is held in the year in which the term expires.

The age limit to serve on the Board is 79. A director who reaches the age limit shall be considered to have automatically resigned as of the date of the next ordinary general meeting, which will note this resignation. Subject to this reservation, directors may always be re-elected.

The Board of Directors carries out the inspections and verifications it deems necessary. The Chairman or the Chief Executive Officer of the Company must communicate to each director all the documents and information necessary to perform his mission.

The Board elects a chairman from among the members, who must be an individual, under penalty of nullification of the election. The Board determines his compensation and the term of office, which may not exceed his term as a director. The Chair of the Board must be less than 75 years old. If this age limit is reached during his term, the Chair of the Board shall be deemed to have automatically resigned from office. His term is extended, however, until the next meeting of the Board of Directors, which will then elect a new Chair.

The Chair organizes and directs the work of the Board and reports on that work to the general meeting of the shareholders. He ensures the correct operation of the corporate bodies and ensures that directors are able to perform their mission.

The Board of Directors meets as often as required by the Company's interest, on a notice from the Chair. In addition, if the Board has not met for more than two months, directors representing at least

one-third of the members of the Board may ask the Chair to call a Board meeting on a specific agenda. The Chief Executive Officer may ask the Chairman to call a meeting of the Board to consider a specific agenda. The notices of meeting are issued by all methods, even verbally. Board meetings are held at the registered office, or at any other location indicated in the notice of meeting. The Board may validly deliberate only if at least half of the members are present. Decisions are made by a majority vote of the members present or represented.

Directors who participate in Board meetings via videoconferencing or electronic methods that allow their identification and effective participation are deemed present for counting the quorum and majority. The nature and conditions of such methods are determined by the regulations in force and subject to the reservations stipulated by said regulations.

The Chair does not have the deciding vote in the event of a tie vote. One or more advisors may assist in an advisory capacity at meetings of the Board of Directors.

Assessment of the operations of the Board of Directors

The Internal Rules of Procedure of the Board of Directors provide that the Board must devote one item on its agenda, at least once a year, to a discussion of its operations.

The annual discussion of the operations of the Board of Directors for 2022 took place in December 2021. In particular, this discussion covered the conditions for preparing Board meetings, the frequency and duration of the meetings, the composition of the Board (diversification of expertise and balance of powers), and the use of an outside expert for technical questions. The Board considered that its operating practices were satisfactory.

Number of shares to be held by the directors

The by-laws stipulate no obligation for directors to own shares.

Changes to the articles of association

Changes to the articles of association are made under the conditions provided for by law.

Limitation of the powers of the Chief Executive Officer (Directeur Général)

The limitations placed by the Board of Directors on the powers of the Chief Executive Officer (*Directeur Général*) are set forth in Article 4 of the Internal Rules of Procedure of the Board, presented below:

Article 4: Exercise of his powers by the Chief Executive Officer

"The following decisions of the Chief Executive Officer are subject to prior authorization by the Board of Directors:

a) Significant decisions to create sites abroad through the setting up of offices, a direct or indirect subsidiary, or through an acquisition of an equity interest, as well as the decisions to withdraw from these sites;
b) Significant transactions that could affect the strategy of the Group or change its financial structure or its scope of activity;

c) *The acquisition or sale of all stakes in any and all companies created or to be formed, the participation in the formation of all companies, groups and organizations, the subscription to all issues of shares, units and bonds;*
d) *Any exchanges, with or without cash balance, of assets, securities or stocks;*
e) *The acquisition or sale of real estate;*
f) *Sureties granted on corporate assets;*
g) *Securing loans exceeding €150,000.*

More generally, the Chief Executive Officer will submit for prior Board approval any significant transaction outside the stated strategy of the company. The significant or non-significant nature of such transactions shall be assessed by the Chief Executive Officer, under his responsibility. "

As of this date, the Company has no Chief Operating Officers.

Statement relating to corporate governance and compliance with the Middlenext code

The Company refers to the Middlenext code of corporate governance. The Board of Directors took note of the items contained under the heading "Points to be watched" of the MiddleNext Code. The recommendations of the MiddleNext Code are all applied by the Company with the one exception mentioned in the table below:

Recommendations of the MiddleNext Code	Explanations for their non-application
(*Recommendation 1*) Each director should attend shareholders' general meetings.	The Company's general meetings are generally attended by fewer than five shareholders. In 2022, 4 shareholders attended the general meetings of June 28 and July 28.
(Recommendation 21) Condition of performance applicable to stock options evaluated over a period of at least 3 years.	The exercise of stock options is contingent on meeting objectives over a shorter time period considered more appropriate by the Board of Directors with respect to its strategic milestone targets.

The table below provides an overview of the Middlenext recommendations.

Recommendations of the MiddleNext Code	In compliance	Plans to comply	Considered unsuitable
R1: Board member ethics	X (1)		
R2: Conflicts of interest	X		
R3: Composition of the board – Independent directors	X		
R4: Board member information	X		
R5: Director training	X		

Recommendations of the MiddleNext Code	In compliance	Plans to comply	Considered unsuitable
R6: Organization of Board and committee meetings	X		
R7: Establishment of committees	X		
R8: Corporate Social Responsibility Committee	X		
R9: Implementing a board of directors' rules of procedure	X		
R10: Selection of each administrator	X		
R11: Board member's term of office	X		
R12: Director's compensation	X		
R13: Implementing an evaluation process for the Board's work	X		
R14: Relations with "shareholders"			X (1)
R15 Diversity and equity policy	X		
R16: Definition and transparency of executive officer compensation	X		
R17: Succession planning for "managers"	X		
R18: Combination of employment contract with a corporate office	X		
R19: Severance benefits	X		
R20: Supplementary pension plans	X		
R21: Stock options and restricted stock units			X (2)
R22: Review of the "Points to be watched"	X		

(1) The directors do not participate in the general meetings due to the small number of shareholders attending (four at the two general meetings of 2022).

(2) Condition of performance applicable to stock options and restricted stock units evaluated over a period of at least 3 years.

3.1.5. Special committees

The Board of Directors has five Committees, whose functions are governed by the rules of procedure of the Board (see section 3.1.4, Rules of Procedure). The directors serving on the committees were considered independent by the Board of Directors in application of the recommendations of the Middlenext code.

Audit Committee

The Audit Committee comprises three directors: Jean-François Labbé, Luzi von Bidder, Lauren Silvernail. It is chaired by Jean-François Labbé. The Chief Executive Officer attends the Audit Committee meetings.

During the 2022 fiscal year, the Audit Committee met five times. The attendance rate at these meetings was 100%. The Audit Committee's work included the review of the budget and revised budget, comparative analysis of the budget and updated data, key closing issues and certain tax issues.

Compensation Committee

The Compensation Committee comprises three directors: Adrienne Graves, Jean-François Labbé, Lauren Silvernail. It is chaired by Adrienne Graves.

During the 2022 fiscal year, the Remuneration Committee met three times. The attendance rate at these meetings was 100%. The work of the Compensation Committee focused in particular on the following subjects: the rules for calculating employee bonuses, the allocation of restricted stock units (*actions gratuites*) and stock options, compensation for the Chief Scientific Officer, the recruitment plan, the increase in payroll for 2022, and compensation for the Chief Executive Officer for 2022.

Corporate Governance Committee

The Corporate Governance Committee comprises three directors: Lauren Silvernail, Luzi von Bidder and Les Kaplan. It is chaired by Ms. Lauren Silvernail.

During the 2022 fiscal year, the Corporate Governance Committee met once. The attendance rate at this meeting was 100%. The Corporate Governance Committee’s work focused in particular on the changes to the MiddleNext corporate governance code, the "recommendations" and " points to watch" of the revised Middlenext corporate governance code, the risks faced by the Company; Board operations; the status of Board members' relationships with the Company, with the members of its Board of Directors and with its Chief Executive Officer; the annual assessment of directors' independence; the annual discussion of conflicts of interest; the succession plan for the Chief Executive Officer and key executives, and the plan in the event of temporary unavailability of the Chief Executive Officer and key executives.

Science and Technology Committee

The Science and Technology Committee is comprised of two directors: Adrienne Graves and Les Kaplan. The Committee is chaired by Les Kaplan.

During 2022, the Science and Technology Committee met four times with an attendance rate of 100%. During these meetings, the Committee discussed, among other subjects, precautions to be adopted in ongoing clinical studies in the context of the COVID 19 epidemic, the follow-up of patient enrollment for the Phase 3 clinical studies on NCX 470, the results of the Phase 2b clinical study on NCX 4251, the preparation of the end-of-Phase 2 meeting with the U.S. FDA for NCX 4251 and potential options for this compound.

Corporate Social Responsibility Committee

Three directors serve on the Corporate Social Responsibility Committee: Lauren Silvernail, Luzi von Bidder and Les Kaplan. It is chaired by Ms. Lauren Silvernail.

The Corporate Social Responsibility met once in 2022. The attendance rate at this meeting was 100%. During this meeting, the Committee examined the consequences of the Company’s activities and strategy on employment, society and the environment.

3.1.6. Conflicts of interest

In accordance with the updated Middlenext corporate governance code and the Board of Directors' internal rules of procedure, the Board of Directors examined in December 2022 the existence of potential conflicts of interest and duly noted that the directors confirmed in writing the absence of conflict of interest as company directors of Nicox SA.

To the Company's knowledge, there are in consequence no potential conflicts of interest between the duties of the directors to the Company and their private interests and/or other interests and positions.

To the Company's knowledge, no loans or guarantees have been made to corporate officers or executives, and the Company does not use assets owned by the officers or executives of the Company or their families.

To the Company's knowledge no company director or executive officer:

- has been convicted of fraud during at least the last five years;
- has been involved in a bankruptcy, receivership or liquidation receiving or been placed in official receivership during at least the last five years;
- has been the subject of any official public sanction for infractions rendered by statutory or regulatory authorities (including designated professional bodies) during at least the last five years;
- has been disqualified by a court of law from serving as a member of the board of directors, executive management or supervisory board or from intervening in the management of the operations of an issuer during at least the last five years.

The lock-up commitments for shares to be issued from the possible exercise of stock options granted to Andreas Segerros are described in section 6 of this report.

No arrangements or agreements have been concluded with the Company's main shareholders or co-contractors whereby any of the persons referred to in section 3.1 of this report have been selected as a member of a management or supervisory body or as Chief Executive Officer. However, it is specified that Mr. Jean-François Labbé was appointed in 2010 at the request of a shareholder, Banque Publique d'Investissement (BPI, formerly Fonds Stratégique d'Investissement).

3.1.7. Management Committee

As of the date of this report, the Company' Management Committee is composed of five persons:

Name	Hiring or first appointment date	Positions held in the Nicox group
Andreas Segerros	2022	Chief Executive Officer
Gavin Spencer (45)	2005	Executive Vice President, Chief Business Officer
Sandrine Gestin	1999	Vice President, Finances
Doug Hubatsch	2021	Executive Vice President, Chief Scientific Officer
Emmanuelle Pierry	2002	General Counsel, Head of Legal Affairs

Biographies of the members of the Management Committee

Andreas Segerros' biography can be found in section 3.1.1 of this annual report.

Gavin Spencer – Executive Vice President, Chief Business Officer – Dr. Spencer has been the Chief Business Officer since 2017. Prior to that he served as Executive Vice President in Charge of Corporate Development since 2012. He joined Nicox in 2005. Prior to joining Nicox, Dr. Spencer served as Senior Manager, new technology and product innovation at Novartis Consumer Health, where he had responsibilities in the identification, evaluation and development of new technologies. Dr. Spencer began his career in the development and evaluation of new products at Boots Healthcare International. Dr. Spencer has more than 25 years of management and operational experience in the life sciences industry across many strategic roles and has been key in building and managing the partnerships, including closing the 2006 Pfizer deal, the 2010 Bausch + Lomb deal, the VISUfarma deal in 2016 and subsequent spin-off, and also initiating our partnership with Ocumension Therapeutics in China. He has also played a key role in spearheading our recent financing activities. Dr. Gavin Spencer holds a B.Sc. in chemistry with first class honors and a Ph.D. in chemistry from the University of Aberdeen.

Sandrine Gestin – Vice President, Finance –Ms. Gestin joined Nicox in 1999 and has held several positions at the company, including chief financial officer, director of accounting and financial controller and more recently Vice President for Finance and CFO. Before joining Nicox, Ms. Gestin spent 10 years at IBM France where she had responsibilities for the consolidation of overseas subsidiaries. Ms. Gestin holds a master's degree in accounting and finance (*maîtrise des sciences et techniques comptables et financières*) from the Institut d'Administration des Entreprises (IAE) of Nice, France.

Doug Hubatsch – Executive Vice President, Chief Scientific Officer

Doug Hubatsch joined Nicox in December 2021. Prior to joining Nicox he was Global Medical Head for Ocular Surface Disease and Digital Medicines within Global Medical Affairs at Novartis Pharmaceuticals. Doug Hubatsch has more than 25 years' experience in Discovery Research, Development and Medical Affairs in Novartis, Alcon, Roche and AstraZeneca and has been involved

with the launch of more than 10 products through his career including Simbrinza (Alcon) for glaucoma and Xiidra (Novartis) for dry eye disease.

Emmanuelle Pierry – General Counsel, Head of Legal – Ms. Pierry has been in charge of legal affairs at Nicox since 2002. Before joining Nicox, Ms. Pierry was a member of the Paris Bar (*Avocat au Barreau de Paris*) for 10 years and practiced business counseling and litigation at international law firms. Mrs. Pierry holds the French Bar diploma (*Certificat d'Aptitude à la Profession d'Avocat*) and degrees in specialized studies in business law from Paris I - Panthéon Sorbonne University (DESS—Master 2 - Paris I) and the Business Law Institute of Paris II, Panthéon - Assas University.

The Company is committed to the principle of equal representation of men and women. Two of the five members of the Management Committee are women.

4. Regulated agreements

There are no agreements within the meaning of Article L. 225-37-4 2° of the French Commercial Code.

5. Compensation of corporate officers

5.1. Compensation and benefits paid or granted to members of the Board of Directors of the Company for fiscal 2022

The following table sets out the compensation paid to directors and other compensation paid to non-executive directors during the years ended December 31, 2022 and December 31, 2021.

Non-executive directors	**FY 2021**		**FY 2022**	
	Compensation payable for 2021	Compensation paid in 2021	Compensation payable for 2022	Compensation paid in 2022
Jean-François Labbé				
Directors' compensation	€60,000	€60,000	€50,000	€50,000
Other compensation	-	-	-	-
Adrienne Graves				
Directors' compensation	€60,000	€60,000	€50,000	€50,000
Other compensation	-	-	-	-
Luzi von Bidder				

Non-executive directors	FY 2021		FY 2022	
Directors' compensation	€60,000	€60,000	€50,000	€50,000
Other compensation	-	-	-	-
Les Kaplan				
Directors' compensation	€60,000	€60,000	€50,000	€50,000
Other compensation	-	-	-	-
Lauren Silvernail				
Directors' compensation	€60,000	€60,000	€50,000	€50,000
Other compensation	-	-	-	-
Michele Garufi				
Directors' compensation	-	-	(1)	-
Other compensation	-	-	-	-
TOTAL	**€300,000**	**€300,000**	**€250,000**	**€250,000**

(1) Michele Garufi waived the €25,000 in compensation that the Board of Directors of December 16, 2022 granted to him for his work as a director for the period from June 1 to December 31, 2022, following his revocation as Chairman and Chief Executive Officer effective May 31, 2022.

Nicox reimburses the directors for travel expenses incurred in attending the meetings of the Board of Directors, namely a total of approximately €44,631 in 2022.

It is should also be noted that none of the Group's directors is eligible for a "golden hello" or for any supplementary pension scheme.

The Company has purchased civil liability insurance covering its directors. This policy is described in section 3.7.1 "Insurance" of this annual report.

In addition, within Nicox Group (See the organization chart in section 6.1 of this annual report), the corporate officers of Nicox Research Institute Srl in office until October 20, 2022 received compensation in respect of their corporate office. Compensation paid for 2022 to these resigning officers amounted to:

- Elizabeth Robinson: €8,333
- Michele Garufi: €8,333

Andreas Segerros who was appointed as sole corporate officer of Nicox Research Institute Srl on October 20, 2022, does not receive any compensation in this capacity.

Summary of past stock option awards to each non-executive officer

The following table provides a summary of past stock option awards to each non-executive officer.

	Plan 7	**Plan 8**
Shareholders' meeting date	May 2017	May 2018
Board of Directors' meeting date	June 08, 2017	May 25, 2018
Total number of shares that may be subscribed	144,000	144,000
Breakdown of shares by corporate officer		
Birgit Stattin Norinder(3)	24,000	24,000
Jean-François Labbé	24,000	24,000
Adrienne Graves	24,000	24,000
Luzi von Bidder	24,000	24,000
Les Kaplan	24,000	24,000
Lauren Silvernail	24,000	24,000
Exercise date of the warrants	(1)	(2)
Expiration date	June 07, 2022	May 24, 2023
Warrant exercise price (€)	11.8841	8.8803
Exercise procedures (when the plan has several tranches)	(1)	(2)
Number of shares subscribed at December 31, 2022	-	-
Aggregate number of equity warrants canceled or expired	144,000	-
Equity warrants remaining at end of year	0	144,000

(1) Exercise of the warrants was conditional on the Company's Board of Directors' determination that the Company completed certain undisclosed strategic objectives, which was the case.

(2) The exercise of the warrants was conditional on the Company's Board of Directors' determination that the Company completed certain undisclosed strategic objectives, which was the case.

(3) Ms. Birgit Stattin Norinder resigned from her position as director in June 2018.

The Company, having consulted its advisors, considers that the issuance of equity warrants to the directors is legally valid and is not equivalent to a stock option grant for the following reasons:

- Unlike an option grant, which is decided by the Board of Directors, the issuance of warrants to the directors is a matter for the general meeting, which alone has powers to make such a decision. In particular, the general meeting designates the beneficiaries by name;

- The features of the warrants differ from those of options. The warrants do not enjoy the favorable tax treatment afforded to options, and are subject to securities regulations.

On September 27, 2018, the Board of Directors undertook, in connection with issues subsequent to the stock warrants for the benefit of non-executive directors of the Company to issue them under market conditions.

Dealings in securities by the Company's directors

None

5.2. Compensation and benefits paid or granted to the Company's Chief Executive Officer for fiscal 2022

Compensation of Andreas Segerros, the Company's Chief Executive Officer since June 1, 2022

As of June 1, 2022, the compensation of Andreas Segerros, in his capacity as Chief Executive Officer of the Company, as voted by the Ordinary Shareholders' Meeting of June 28, 2022, includes the following components:

(A) Fixed annual compensation
400.000*(pro rata temporis* in 2022, beginning June 1, 2022)

(B) Annual variable compensation
Up to 50% of the annual fixed remuneration *(pro rata temporis* in 2022, beginning June 1, 2022). The amount is calculated in reference to the attainment of the Company's objectives for 2022 set by the Board of Directors at its meeting on February 15, 2022.
On January 13, 2022, the Board of Directors considered these objectives to have been fully met. On that basis, Andreas Sergerros' variable compensation for 2022 amounted to €117,260.

(C) Benefits in kind / Pension plan
Benefits in kind:

- Compulsory supplemental health insurance

Pension plan:

- Coverage under the compulsory pension plan (tranches A to C)

(D) Severance benefits
Should Andreas Segerros' appointment as Chief Executive Officer of the Company be terminated, he shall be entitled to a severance payment, except in the case of dismissal for gross misconduct.
This payment shall be subject to a determination by the Board of Directors that at least 50% of the Company's objectives were met for the year preceding his revocation.

The value of the severance payment would correspond to one year of compensation, including both fixed and variable annual compensation, calculated on the basis of compensation owed for the last fiscal year ended preceding the date of dismissal.

(E) Stock option grant

On July 1, 2022, the Board of Directors granted Andreas Segerros, Chief Executive Officer, under the terms of resolution eleven of the Extraordinary Shareholders' Meeting of April 28, 2021, 860,000 stock options, with each option giving a right to subscribe for one new share with a par value of €1.7954, representing the weighted average share price over the twenty trading days preceding the date of the Board meeting, without any discount.

These options will be exercisable in three tranches:

(i) a tranche of 286,666 options exercisable as of June 1, 2023, if the Board determines that at least 50% of the company's 2022 objectives have been achieved,

(ii) a tranche of 286,666 options exercisable as of June 1, 2024 if the Board has determines that the Company has a cash runway of 12 months as of December 31, 2023,

and**(iii**) a tranche of 286,668 options exercisable as of June 1, 2024 if the Board determines that the Company has a cash runway of 12 months as of December 31, 2024.

Should the conditions of performance not be met for any of the three tranches, half of the rights granted for the tranche in question (i.e. 50% of the stock options granted plus one) will be cancelled, with the other half of the rights remaining in force.

- This grant is subject to the conditions set out in the regulations of the May 5, 2021 plan, with the exception of the condition of presence, which will be waived for the first tranche and will apply in all circumstances for the second and third tranches, notwithstanding any clause to the contrary in the regulations of the aforementioned plan.

The Board has required that 10% of the shares obtained by exercising the 860,000 stock options granted to Andreas Segerros must be held in registered form until he ceases to be the Company's Chief Executive Officer.

Compensation of Michele Garufi, Chairman and Chief Executive Officer of the Company until May 31, 2022

On May 13, 2022, the Board of Directors terminated the appointment of Michele Garufi as Chairman and Chief Executive Officer, effective May 31, 2022. Michele Garufi served as interim Chairman of the Board from June 1 to July 28, 2022, pending an amendment to the Articles of Association to permit the appointment of Jean-François Labbé as Chairman of the Board of Directors by extending the age limit for this position to 75. Michele Garufi received no compensation for serving as the Board's interim Chairman. In addition, he waived the € 25,000 compensation for the performance of his duties as a director between June 1 and December 31, 2022.

Michele Garufi received €145,833 in fixed compensation for fiscal 2022 (May 1 to 31, 2022). In 2023 he will also receive €72,397 in variable compensation. Michele Garufi also received €16,667 in

compensation as a corporate officer of Nicox Research Institute Srl for the period from January 1 to October 20, 2022, the date of his resignation from this office.

Benefits in kind for the use of a company car amounted to €2,557 for fiscal 2022.

Under the terms of a resolution of the Board of Directors of April 27, 2021, Michele Garufi was to receive a contractual severance payment equal to two years' compensation, including both the fixed and variable components, based on the amount paid in the fiscal year preceding the date of the revocation, i.e. fiscal 2021. This payment is subject to fulfillment of two conditions: (i) revocation by the Board from his office as Chief Executive Officer or Chairman of the Board of Directors, except for grounds of serious misconduct; and (ii) the determination that the condition of performance of having at least one product approved which generates, directly or indirectly, revenue for a Group entity has been met at the date of revocation.

On May 13, 2023, the Board of Directors decided to revoke Michele Garufi's term of office and determined that all conditions had been met for the payment of this indemnity, which was authorized by the Ordinary General Meeting of June 28, 2022.

Based on a fixed compensation paid in 2021 of €350,000 and a variable compensation paid in 2021 of €160,000, Michele Garufi received a termination payment of €1,020,000.

On May 13, 2022, the Board also decided to waive the condition of presence applicable to Michele Garufi's outstanding stock options, and namely:

Grant date	Options granted	Exercise price	Exercise date	Expiry date
02/12/19	30,000	6.0546	02/12/21	02/12/27
01/14/20	145,000	4.79	01/27/22	01/27/28
01/14/21	135,000	3.5181	01/14/23	01/14/29
02/15/22	135,000	2.3716	02/15/24	02/15/30

Michele Garufi retired from his positions as an officer of Nicox Ophthalmics, Inc on July 12, 2022 and as an officer of Nicox Research Institute, Srl on October 20, 2022.

Dealings in securities by the Chief Executive Officer

The Company is not aware of any security transactions by Andreas Segerros or Michele Garufi.

Total amounts set aside or accrued by the Company or its subsidiaries to provide pension, retirement or other benefits

Pension contributions paid on behalf of Andreas Segerros during the year amounted to € 38,154 and € 32,703 for Michele Garufi for the period from January 1 to May 31, 2022.

6. Information on the capital

The amount of issued capital, the total of the issuer's authorized share capital, the number of shares issued an fully paid and issued but not fully paid, the par value per share and a reconciliation of the number of shares outstanding at the beginning and the end of the year

Share capital: €50,156,698
Number of ordinary shares at April 28, 2023: 50,156,698
Par value of each ordinary share: €1

At December 31, 2022, the data were as follows:
Share capital: €50,100,448
Number of ordinary shares: 50,100,448
Par value of each ordinary share: €1

Number of shares not representing capital and their main characteristics

There are no shares that are not representative of the capital.

6.1. Breakdown of the share capital and voting rights

Based on notifications of crossing thresholds received by the Company, and notably the thresholds set out in the articles of association (2% or more) and by law, and on a non-diluted basis, share ownership before dilution is as follows:

Shareholders	As of December 31, 2022			As of December 31, 2021		
	Number of shares	% of capital	% of voting rights	Number of shares	% of capital	% of voting rights
HBM Healthcare Investments	2,722,947	5.43	5.43	2,619,102	6.07	6.07
Armistice Capital	6,849,316	13.67	13.67	2,570,024[(1)]	5.96	5.96
Treasury shares	288,965	0.58	0.58	211,967	0.49	0.49
Public	40,239,220	80.32	80.32	36,701,481	85.08	85.08
Total	**50,100,448**	**100**	**100**	**43,138,185**	**100**	**100**

*On the date of this Annual Report, Mr. Garufi held 592,051 shares.

(1) On April 13, 2022, Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 2% threshold of the Company's capital and voting rights on April 6, 2022, and holding in consequence, on behalf of said funds, 836,551 shares of the Company representing an equivalent number of voting rights or 1.935% of the Company's share capital and voting rights.

HBM Healthcare Investments (Cayman) Ltd, became a shareholder of Nicox through the private placement made by the Company in August 2016. HBM Healthcare Investments (Cayman) Ltd,

incorporated in the Cayman Islands having its registered office at Governors Square, Suite #4-212-2, 23 Limie Tree Bay Avenue, West Bay, Grand Cayman, Cayman Islands, is a subsidiary of the company.

Other than those mentioned in section 6.1 of this Annual Report, no shareholder has reported holding more than 2% of the share capital or voting rights. To the Company's knowledge, the shareholders have not entered into any agreement or concerted action. It should be noted that, in view of the current ownership structure, the Company has not implemented special measures to ensure that control of its capital is not exercised abusively.

The Company is not able to disclose the approximate number of shareholders. Information available to the Company regarding the number of shares held by its employees is presented in section6.2 "Capital held by employees" of this Annual Report.

As of April 27, 2023,, the Company held 299,367 own shares in connection with a liquidity agreement with Kepler Cheuvreux providing for market making services for the Company’s shares.

In addition, at April 27, 2023, if all instruments giving access to the share capital awarded and outstanding were exercised and all restricted stock units were fully vested, 18,197,846 new shares would be issued, resulting in a dilution equal to 36.28% based on the share capital on this date and 26.62% on a fully-diluted basis.

The reader is invited to refer to the summary of dilutive instruments presented in section 19.3 "Summary of dilutive instruments" of this annual report.

6.2. Capital held by employees and rights giving access to capital

6.2.1. Shares of the Company

The Company has no knowledge of employee shareholdings apart from the insignificant percentage of shares listed in the share register held by certain Group employees.

6.2.2. Restricted stock units (*actions gratuites* or free shares)

A summary of restricted stock units outstanding at December 31, 2022 is presented in note 16.3 to the consolidated financial statements.

In 2022, 959,700 restricted stock units (*actions gratuites*) were awarded to Group employees (Nicox SA, Nicox Research Institute SRL and Nicox Ophthalmics Inc.) pursuant to decisions of the four Board of Directors' meetings.

Restricted stock units awarded to and acquired by during the year the ten employee beneficiaries (excluding directors and officers) having received the highest number thereof:

Restricted stock units awarded during the year to the ten employee beneficiaries (excluding directors and officers) having received the highest number thereof	Number of restricted stock units granted/vested shares/transferable shares	January 27, 2020	August 5, 2020	October 15, 2020	January 12, 2022	February 15, 2022	July 19, 2022	September 23, 2022
Restricted stock units during the year to the ten employee beneficiaries (excluding directors and officers) of the Company and its subsidiaries who received the highest number thereof (aggregate figures)	694,500	0	0	0	9,000	80,500	550,000	55,000
Restricted stock units of the Company finally vested during the year by the ten employees of the Company and its subsidiaries receiving the largest number (aggregate figures)(1)	77,497	49,500	12,000	15,997	0	0	0	0

(1) 14 beneficiaries are taken into account in this calculation to take into account acquisitions of the same amounts

6.2.3. Stock options

A summary of stock options outstanding at December 31, 2022 is presented in note 16.1 to the consolidated financial statements.

In 2022, 2,541,800 stock options were awarded to Group employees (Nicox S.A., Nicox Research and Nicox Ophthalmics) pursuant to decisions of two Board of Directors' meetings, giving them the right to subscribe for 2,541,800 shares.

In the 2022 no stock options were exercised.

Options to purchase or subscribe shares granted to and exercised by ten employee beneficiaries who are not corporate officers

Options to purchase or subscribe shares granted to and exercised by ten employee beneficiaries who are not corporate officers (1)	Total number of shares granted / subscribed or purchased	Weighted average price	February 15, 2022	April 7, 2022	July 19, 2022
Options granted during the year by the issuer, and by any company within the scope of the option grant, to the ten employees of the issuer and any company within that scope receiving the largest number of options	938,000	€2.09	214,500	126,500	597,000
Options to buy shares in the issuer and the foregoing companies exercised during the year by the ten employees of the issuer and those companies who bought or subscribed to the largest number of shares (aggregate figures)	0	€0.00	0	0	0

(1) One right = one action

6.3. Shareholdings of corporate officers

The equity interests held by corporate officers in the Company's capital are detailed below:

Name of Corporate Officer	Number of shares held as of April 27, 2023
Michele Garufi	592,051
Adrienne Graves	-
Jean-François Labbé	-
Les Kaplan	82,034
Luzi von Bidder	10,000
Lauren Silvernail	-
Andreas Segerros	-
TOTAL	**684,085**

At April 15, 2023, to the best of the Company's knowledge, its administrative and executive management bodies held 684,085 shares, i.e., 1.22% of the capital and voting rights based on the number of shares outstanding at March 31, 2023, the date of the most recent declaration of voting rights (Article 223-16 of the AMF's General Regulations).

6.4. Thresholds defined by the Articles of Association and/or the law crossed during the financial year ended December 31, 2022

During the year ended December 31, 2022, the Company received the following threshold crossing disclosures:

- on January 27, 2022, , Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 5% threshold of the Company's capital and voting rights on January 21, 2022, and holding in consequence, on behalf of said funds, 2,140,000 shares of the Company representing an equivalent number of voting rights or 4.961% of the Company's share capital and voting rights.

- on March 10, 2022, , Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 4% threshold of the Company's capital and voting rights on March 03, 2022, and holding in consequence, on behalf of said funds, 1,720,000 shares of the Company representing an equivalent number of voting rights or 3.979% of the Company's share capital and voting rights.

- on April 13, 2022, , Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 2% threshold of the Company's capital and voting rights on April 06, 2022, and holding in consequence, on behalf of said funds, 836,551 shares of the Company representing an equivalent number of voting rights or 1.935% of the Company's share capital and voting rights.

- On November 29, 2022, , Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the thresholds of 2%, 4%, 6%, 8%, 10% and 12% of the Company's capital and voting rights on November 25, 2022, and holding in consequence, on behalf of said funds, 6,849,316 shares of the Company representing an equivalent number of voting rights or 13.671% of the Company's share capital and voting rights.

- On November 29, 2022, HBM Healthcare Investments (Cayman) Ltd reported having crossed above the 6% threshold of the Company's capital and voting rights on November 25, 2022, and

holding on behalf of the said funds, 2,722,947 shares representing the same number of voting rights, i.e. 5.43% of the capital and voting rights of the Company.

In addition, since the beginning of 2023, the Company was notified that the following thresholds had been crossed:

- On January 20, 2023, HBM Healthcare Investments (Cayman) Ltd reported having crossed above the 5% threshold of the Company's capital and voting rights on January 18, 2023, and holding on behalf of the said funds, 2,494,490 shares representing the same number of voting rights, i.e. 4.98% of the capital and voting rights of the Company.

- On January 25, 2023,, Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 12% threshold of the Company's capital and voting rights on January 19, 2023, and holding in consequence, on behalf of said funds, 6,001,336 shares of the Company representing an equivalent number of voting rights or 11.979% of the Company's share capital and voting rights.

- On March 02, 2023,, Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 10% threshold of the Company's capital and voting rights on February 24, 2023, and holding in consequence, on behalf of said funds, 4,921,882 shares of the Company representing an equivalent number of voting rights or 9.813% of the Company's share capital and voting rights.

- On April 14, 2023, Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 8% threshold of the Company's capital and voting rights on April 06, 2023, and holding in consequence, on behalf of said funds, 4,004,471 shares of the Company representing an equivalent number of voting rights or 7.984% of the Company's share capital and voting rights.

- On April 20, 2023,, Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 6% threshold of the Company's capital and voting rights on April 14, 2023, and holding in consequence, on behalf of said funds, 2,891,045 shares of the Company representing an equivalent number of voting rights or 5.764% of the Company's share capital and voting rights.

- On April 25, 2023,, Armistice Capital, LLC, acting on behalf of Armistice Capital Master Fund Ltd., reported having crossed below the 5% threshold of the Company's capital and voting rights on April 20, 2023, and holding in consequence, on behalf of said funds, 2,484,550 shares of the Company representing an equivalent number of voting rights or 4.954% of the Company's share capital and voting rights.

6.5. Thresholds under the articles of association - Voting rights

Under Article 10.2 of the articles of association, any individual or legal entity acting alone or in concert who owns in any form whatsoever, pursuant to articles L. 233 7 *et seq*. of the French commercial code a number of shares representing immediately or in the future a fraction equal to 2% of the capital and/or rights in the Company allowing them to vote in shareholders' meetings, or any multiple of that percentage up to 50% and even if that multiple crosses the legal threshold of 5%, shall inform the Company of the total number of shares owned by it by registered letter with return receipt,

sent to the head office within four trading days from the date the threshold is crossed, or by any other equivalent means for shareholders or the holders of bearer shares residing outside France.

This disclosure requirement applies under the same conditions as those described above whenever a portion of the share capital or voting rights owned falls below any of the thresholds described above.

If the above stipulations are not followed, then any shares exceeding the reporting threshold shall be denied the right to vote if this is requested by one or more shareholders owning together or separately at least 2% of the capital and/or voting rights in the Company, under the conditions referred to in Article L.233-7, paragraph 6 of the French commercial code.

In the event of an adjustment, the corresponding voting rights may not be exercised until the deadline provided by existing laws and regulations expires.

6.6. Dealings by managers in the Company's own shares

The Company has no knowledge of any security transactions carried out by senior executives.

6.7. Company control

No person or entity has control of the Company, whether jointly or separately or directly or indirectly.

6.8. Pledges of the Company

Refer to note 4.3 of the Consolidated Financial Statements.

6.9. Agreements providing for payments to be made to members of the Board of Directors or to employees

There are no agreements providing for the payment of severance benefits to members of the Board of Directors.

Undertakings assumed with respect to the Chief Executive Officer and members of the Management Committee are described in note 27.2 to the consolidated financial statements.

6.10. Rules governing the appointment and replacement of directors and amending the articles of association

6.10.1. Rules governing the appointment and replacement of directors

The rules governing the appointment and replacement of members of the Board of Directors are described in the section 3 "Corporate Governance" of this Annual Report.

6.10.2. Rules governing amendments of the articles of association

Pursuant to Article L225-96 of the French commercial code, only the extraordinary general meeting has the authority to amend the Company's articles of association.

However, whenever the Company's head office is transferred by decision of the Board of Directors, then the Board is authorized to amend the articles of association accordingly.

6.10.3. Powers of the Board of Directors

The powers of the Board of Directors are described in section 3 "Corporate Governance" of this Annual Report.

6.11. Table summarizing the delegations of authority in force

The ordinary general meeting of July 28, 2022 delegated its authority and/or powers to the Board of Directors under the following conditions:

Authorizations granted to the Board of Directors by the extraordinary general meeting of July 28, 2022	Maximum nominal amount of the capital increase (in euros)	Length of the delegation of authority with effect from the date of the extraordinary general meeting of July 28, 2022	Use of the delegation of authority on the date of this report.
Delegation of authority to the Board to issue shares, equity securities giving access to other equity securities of the Company or rights to the allotment of debt securities as well as securities giving access to equity securities of the Company to be issued, maintaining shareholders' preferential subscription rights (resolution 1).	20,000,000	26 months	-
Delegation of authority granted to the Board of Directors to issue shares, equity securities giving access to other equity securities of the Company or rights to the allotment of debt securities as well as securities giving access to equity securities to be issued, canceling shareholders' preferential subscription rights, and through a public offer than those covered by article L. 411-2 1° of the French Monetary and Financial Code (*Code monétaire et financier*) (resolution 2).	15,000,000*	26 months	-
Delegation of authority to the Board of Directors to issue shares, equity securities giving access to other equity securities of the Company or rights to the allotment of debt securities as well as securities giving access to equity securities to be issued, canceling shareholders' preferential subscription rights, and through a public offer	15,000,000*	26 months	

Authorizations granted to the Board of Directors by the extraordinary general meeting of July 28, 2022	Maximum nominal amount of the capital increase (in euros)	Length of the delegation of authority with effect from the date of the extraordinary general meeting of July 28, 2022	Use of the delegation of authority on the date of this report.
covered by article L. 411-2 1° of the French monetary and financial code (resolution 3).			
Authorization to set the issue price for the securities to be issued under the second and third resolutions within the limit of 10% of the share capital per year (resolution 4).	n/a	26 months	-
Authorization to increase the number of shares to be issued in connection with issues, with or without preferential subscription rights, in application of the first, second, third, fourth and eighth resolutions (resolution°5).	15 % of the initial issue**	26 months	-
Delegation of authority to increase the share capital by the capitalization of reserves, earnings, additional paid-in premiums or other eligible amounts (resolution 6).	n/a	26 months	-
Delegation of authority to increase the share capital in view of consideration for contributions in kind granted to the Company, excluding the case of a public exchange offer (resolution 7).	10 % of the share capital on the issue date*	26 months	-
Delegation of authority to increase the capital for the benefit of a selected category of beneficiaries, canceling the preferential subscription rights of shareholders for their benefit (resolution° 8) (2).	15,000,000*	18 months	13,698,632

Authorizations granted to the Board of Directors by the extraordinary general meeting of July 28, 2022	Maximum nominal amount of the capital increase (in euros)	Length of the delegation of authority with effect from the date of the extraordinary general meeting of July 28, 2022	Use of the delegation of authority on the date of this report.
Delegation of authority to increase the share capital for the benefit of participants of a company savings plan with cancellation of the preferential subscription rights of shareholders for their benefit (resolution 9).	60,000 (1)	26 months	-
Authorization given to the Board of Directors to award restricted stock units for existing or future shares, entailing waiver *ipso jure* by shareholders of their preferential subscription rights (resolution 10)	1,000,000	38 months	302,815
Authorization to grant options conferring a right to subscribe for new shares of the Company or purchase existing shares, entailing waiver ipso jure by shareholders of their preferential subscription rights (resolution 11).	2,500,000	38 months	655,571

* To be deducted from the initial nominal ceiling of €15,000,000 set in the second resolution, in turn to be deducted from the total maximum nominal amount of the capital increase of €16,500,000.
** To be deducted from the nominal limit of the capital increase set by each of the resolutions under which the initial issue was decided.
(1)Deducted from the total maximum nominal amount of €20,000,000
(2) The category of beneficiaries is as follows: (i) one or more companies or collective investment schemes under French or foreign law investing in the pharmaceutical/biotechnology sector, (ii) natural persons investing on a regular basis in the pharmaceutical/biotechnology sector and/or (iii) one or more financial institutions or any authorized investment services provider undertaking to acquire the shares for resale to the persons mentioned above under (i)

7. Corporate social responsibility

7.1. Discrimination and diversity

The size of the company and the closeness of the teams mean that the Company has encountered no problems of discrimination and diversity, either on hiring or in the day-to-day management of the teams.

However, in order to prevent all forms of discrimination, the HR manager clearly states in the internal rules (Handbook) introduced in countries where Nicox has employees, that fighting discrimination and

promoting diversity are major priorities for its human resources management. The company has also established and equal opportunity and inclusion policy.

The introduction of these internal rules provides the Company with an opportunity to remind its employees of the importance of respect for fundamental principles and to impose sanctions if necessary.

7.2. Greenhouse gas emissions

As yet, the Company has no environmental charter in place but is committed daily through various initiatives to combating the emission of greenhouse gases, such as for example:

- The introduction of carpooling for business travel (travel between Sophia Antipolis in France and Bresso in Italy);
- Teleworking. An agreement was concluded with labor partners in 2018 (replacing the agreement of 2014);
- An eco-driving guide attached to the Car Policy;
- Restriction on the engine size of company cars.

The Company is keenly aware of the importance of social, societal and environmental issues.

We have procedures in place to govern the way we conduct our business which include gender equality, inclusion and anti-corruption measures. We reviewed our service providers' statements on gender equality, inclusion and combating corruption and the overwhelming majority of our service providers have implemented policies in these areas.

Nicox outsources the development of its compounds (synthesis, formulation and manufacturing of molecules and products, non-clinical studies and clinical studies). We have adopted sustainable development measures in our offices.

Although we have little influence on the environmental policies of our subcontractors because of the size of our company, we do review and consider these issues for our major suppliers, including in the selection process. Our key subcontractors declare that they have policies in place to reduce their environmental impact, and those that do not have such policies have undertaken to do so in the near future. Some have been evaluated by environmental rating agencies, achieving high scores, and others provide reports in accordance with international sustainability assessment standards. Some service providers have given us detailed reports on their progress in certain key areas.

8. Auditors' special report on regulated agreements

Approbans Audit

Ernst & Young Audit

Nicox S.A.

Annual general meeting to approve the financial statements for the year ended December 31, 2022.

Statutory Auditors' special report on regulated agreements

Approbans Audit
22, boulevard Charles Moretti
La Palmeraie du Canet
13014 Marseille
S.A.R.L. with share capital of € 100 000
Companies Register (RCS) No °5 525 098 786 Marseille

Statutory Auditors
Member of the Regional Association of Chartered Accountants
of Aix-Bastia

Ernst & Young Audit
Tour First
TSA 14444
92037 Paris-La Défense cedex
S.A.S with variable capital
Companies Register (RCS) No.°344 366 315. Nanterre

Statutory Auditors
Member of the Regional Association
of Chartered Accountants of Versailles and the Central
Region

This is an unsigned free translation into English of the original report issued in the French language and it is provided solely for the convenience of English speaking users. This report should be read in conjunction with, and construed in accordance with, French law and professional standards applicable in France.

Nicox S.A.

Annual general meeting to approve the financial statements for the year ended December 31, 2022.

Statutory Auditors' special report on regulated agreements

To Nicox SA's General Meeting:

In our capacity as Statutory Auditors of your Company, we hereby report on regulated agreements.

We are required to inform you, on the basis of the information provided to us, of the essential terms and conditions, and also the reasons justifying the relevance to the company, of those agreements and commitments indicated to us or apprised by us during the course of our engagement, without being required to comment as to whether they are beneficial or appropriate or to ascertain the existence of other agreements and commitments. It is your responsibility, pursuant to Article R. 225-31 of the French commercial code, to evaluate the merits of these agreements and commitments with a view to their approval.

Our role is also to provide you with the information stipulated in Article R. 225-31 of the French Commercial Code on agreements previously approved by the General Meeting, if any, in force during the period.

We have implemented the measures considered necessary by us to comply with the professional guidance issued by the French National Institute of Statutory Auditors *(Compagnie Nationale des Commissaires aux Comptes)* in relation to this type of assignment.

Agreements submitted for approval to the general meeting

We hereby inform you that we were not notified of any agreement or commitment authorized during the past financial year to be submitted to the general meeting for approval in accordance with the provisions of Article L. 225-38 of the French commercial code

Agreements already approved by the General Meeting

We inform you that we have not been advised of any agreement or commitment already approved by the general meeting remaining in force in the period under review.

Marseille and Paris-La Défense, April 28, 2023

Statutory Auditors

French original signed by:

Approbans Audit	Ernst & Young Audit
Pierre Chauvet	Pierre Chassagne

CONSOLIDATED FINANCIAL STATEMENTS AT DECEMBER 31, 2022

Nicox S.A.

2405, route des Dolines, Drakkar D,

06560 Valbonne Sophia Antipolis, France

Grasse Companies Register (RCS) No.: 403 942 642

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Consolidated financial statements for the period ended December 31, 2022 with comparative data at December 31, 2021

Consolidated statement of profit or loss

	Notes	2022	2021
Revenue from collaborations	**5.2**	**5,242**	**8,583**
Royalty payments	**5.3**	(1,971)	(1,350)
Net profit	**5.4**	**3,271**	**7,233**
Research and development expenditures	**5.5**	(17,992)	(17,910)
Administrative expenses	**5.6**	(7,479)	(7,000)
Other income	**5.7**	762	843
Other expenses	**5.8**	(1,753)	(211)
Operating loss before amortization and impairment of intangible assets		**(23,191)**	**(17,045)**
Amortization of intangible assets	**9.1**		(1,205)
Impairment of intangible assets	**4.6**	(10,870)	(27,760)
Operating loss		**(34,061)**	**(46,010)**
Financial income	**5.9.2**	6,062	3,456
Financial expenses	**5.9.2**	(2,288)	(4,851)
Net financial income/(expense)	**5.9.2**	**3,774**	**(1,395)**
Loss before tax		**(30,287)**	**(47,405)**
Income tax (expense) / benefit	**6 / 21**	2,528	3,644
Loss for the period		**(27,759)**	**(43,761)**
Loss per share (in €)	**7**	**(0.63)**	**(1.17)**
Basic/diluted loss per share (in €)	**7**	(0.63)	(1.17)

Consolidated statement of other comprehensive income

	Notes	2022	2021
Loss attributable to equity holders		**(27,759)**	**(43,761)**
Exchange differences on translation of foreign operations		1,711	2,994
Other comprehensive income/(loss) to be reclassified to profit or loss in subsequent periods (net of tax)		**1,711**	**2,994**
Actuarial gains and losses	**18**	134	2
Other comprehensive loss not to be reclassified to profit or loss in subsequent periods (net of tax)		**134**	**2**
Other comprehensive income/(loss) for the period, net of tax, attributable to equity holders of the Company		**1,845**	**2,996**
Total comprehensive loss for the period attributable to equity holders of the Company		**(25,914)**	**(40,765)**

Consolidated statement of financial position

ASSETS	Notes	2022	2021
Non-current assets			
Goodwill	**10**	27,223	25,637
Intangible assets	**9**	31,692	39,974
Property, plant and equipment	**8**	240	1,023
Non-current financial assets	**13**	325	237
Total non-current assets		**59,480**	**66,871**
Current assets			
Trade receivables		2,639	1,086
Government grants receivable	**11**	504	1,452
Other current assets	**12**	1,279	377
Prepayments	**12**	1,612	2,853
Cash and cash equivalents	**14**	27,650	41,970
Total current assets		**33,684**	**47,738**
TOTAL ASSETS		**93,164**	**114,609**

LIABILITIES			
Shareholders' equity			
Issued capital	**15**	50,100	43,138
Share premium		538,202	536,200
Translation reserve		7,665	5,953
Treasury shares		(978)	(847)
Accumulated deficit		(542,556)	(508,892)
Total equity		**52,433**	**75,552**
Non-current liabilities			
Non-current financial liabilities	**20**	24,606	21,160
Deferred tax liabilities	**21**	7,341	9,236
Provisions	**17; 18**	578	661
Total non-current liabilities		**32,525**	**31,057**
Current liabilities			
Current financial liabilities	**20**	828	346
Trade payables		3,102	3,649
Deferred income	19	2,183	1,970
Other current liabilities	**22**	2,093	2,035
Total current liabilities		**8,206**	**8,000**
TOTAL EQUITY AND LIABILITIES		**93,164**	**114,609**

Consolidated statement of cash flows

	Notes	2022	2021
CASH FLOWS FROM OPERATING ACTIVITIES			
Loss for the period		**(27,759)**	**(43,761)**
Adjustments to reconcile the loss for the period to net cash flows			
Amortization, depreciation, and impairment	**8.1; 9.1**	11,216	29,421
Expenses related to share-based payments	**16**	1,182	1,463
Provisions	**17; 18**	51	(67)
Deferred tax liabilities	**6; 21**	(2,498)	(3,679)
Capitalized interests	**4.1**	(169)	189
Change in fair value of put options	**5.9.2**	(3,039)	
Gain on disposal of assets		102	(8)
Losses from disposals / impairment of the bond loan			2,784
Non-cash translation adjustments		(1,911)	(2,276)
Working capital adjustments:		**(22,825)**	**(15,934)**
(Increase) / Decrease in trade receivables and other currents assets		(973)	274
(Increase) / Decrease in government grant receivables	**11**	948	(716)
Increase / (Decrease) in trade payables and other current liabilities		(488)	1,098
Increase / (Decrease) deferred income		213	(3,203)
Change in working capital requirement		**(300)**	**(2,547)**
CASH FLOWS FROM (USED IN) INVESTING ACTIVITIES			
(Purchase) /Disposal of financial assets	**4.1**	174	(167)
Purchase of intangible assets	**9**		-
(Purchase) /Disposal of financial assets	**8**	(42)	(8)
Net cash flows from (used in) investing activities		**132**	**(175)**
CASH FLOWS FROM (USED IN) FINANCING ACTIVITIES			
Proceeds from the issuance of new shares	**15**	8,964	13,713
Treasury shares		218	91
Increase / (Decrease) of borrowings net of issuance costs	**20**	(165)	-
Repayment of finance lease liabilities		(374)	(395)
Net cash flows from (used in) financing activities		**8,643**	**13,409**
Net (Decrease) / Increase in cash and cash equivalents		**(14,350)**	**(5,246)**
Cash and cash equivalents at January 1	**14**	**41,970**	**47,195**
Net foreign exchange difference		30	21
Cash and cash equivalents at December 31	**14**	**27,650**	**41,970**

Consolidated statement of changes in equity

	Issued capital								
	Ordinary shares	Amount	Share premium	Treasury shares	Translation reserve	Reserves	Loss for the period	Attributable to equity holders of the Company	Total equity
At January 1, 2021	**37,030,335**	**37,030**	**528,595**	**(605)**	**2,959**	**(449,046)**	**(18,099)**	**100,835**	**100,835**
Loss for the period							(43,761)	(43,761)	(43,761)
Other comprehensive income/(loss)					2,994	2		2,996	2,996
Comprehensive income/(loss) for the period					**2,994**	**2**	**(43,761)**	**(40,765)**	**(40,765)**
Allocation of profit of the previous period						(18,098)	18,098		
Issuance of ordinary shares	6,000,000	6,000	7,712					13,712	13,712
Share-based payments	107,850	107	(107)			1,463		1,463	1,463
Equity warrants on a loan agreement				(242)				(242)	(242)
Equity component of convertible bonds						549		549	549
At December 31, 2021	**43,138,185**	**43,138**	**536,200**	**(847)**	**5,953**	**(465,131)**	**(43,762)**	**75,552**	**75,552**
Loss for the period							(27,759)	(27,759)	(27,759)
Other comprehensive income/(loss)					1,712	134		1,846	1,846
Comprehensive income/(loss) for the period					**1,712**	**134**	**(27,759)**	**(25,913)**	**(25,913)**
Allocation of profit of the previous period						(43,762)	43,762		
Issuance of ordinary shares	6,849,316	6,849	2,115					8,964	8,964
Share-based payments	112,947	113	(113)			1,182		1,182	1,182
Treasury shares				(131)				(131)	(131)
Put on ABSAs (shares with warrants attached)						(7,221)		(7,221)	(7,221)
At December 31, 2022	**50,100,4**	**50,100**	**538,202**	**(978)**	**7,665**	**(514,798)**	**(27,759)**	**52,433**	**52,433**

Notes to the consolidated financial statements

1. CORPORATE INFORMATION ON THE REPORTING ENTITY

Nicox S.A. (the "Company") is incorporated and domiciled in France. The Company's headquarters is located at 2405 route des Dolines, Drakkar 2, Bât D, 06560 Valbonne. Nicox is listed on Euronext Paris (COX.PA) and has a center for research and pre-clinical development in Italy and a business development office in the United States.

1.1 Summary of the Company's core activities

- Nicox S.A. is an ophthalmology company developing innovative solutions to help maintain vision and improve ocular health. Nicox has a phase 3 clinical development program in glaucoma (the first study has been completed, the second is ongoing), a drug candidate in preclinical development in retinal diseases, a drug candidate in development for dry eye disease with a partner, licensed for the Chinese market, and two licensed products marketed by exclusive partners.

- NCX 470, a novel nitric oxide (NO)-donating bimatoprost eye is in phase 3 clinical development for the reduction of IOP in patients with open-angle glaucoma and ocular hypertension. Mont Blanc, the first of the two Phase 3 clinical trials, has been completed and the results announced in October 2022. The second Phase 3 clinical trial, Denali, is currently ongoing, and the results are expected in 2025. Mont Blanc and Denali trials have been designed to fulfill the regulatory requirements for safety and efficacy Phase 3 trials to support NDA submissions in the U.S. and China. Two new Phase 3b clinical trials to evaluate the dual mechanism of action (NO and prostaglandin analog) in IOP lowering and the potential retinal benefits of NCX 470 are planned to start in H1 2023. Nicox is seeking partnerships for NCX 470 for the U.S. and Japanese markets. NCX 470 has an exclusive licensing agreement with Ocumension Therapeutics for China and Southeast Asia.

- NCX 1728, an NO-donating phosphodiesterase-5 (PDE5) inhibitor, the lead compound of a new class of NO-donating molecules based entirely on NO-mediated activity. NCX 1728 is currently under preclinical evaluation for development in retinal diseases.

- NCX 4251, a novel, patented, ophthalmic suspension of fluticasone propionate nanocrystals in clinical development stage for dry eye disease. Future development of NCX 4251 in the U.S. will require a manufacturing scale-up followed by two additional clinical efficacy studies, each evaluating a sign and symptom of dry eye disease, long-term safety data, and certain additional clinical and non-clinical data to support a New Drug Application (NDA) in the U.S. The Company is seeking a partner to continue the development of NCX 4251 for the U.S. market. NCX 4251 is the subject of an exclusive licensing agreement with Ocumension Therapeutics for China.

- VYZULTA®, indicated for the reduction of IOP in patients with open angle glaucoma or ocular hypertension, is exclusively worldwide licensed to Bausch + Lomb. VYZULTA is marketed in over 15 countries, including the United States and is also approved in a number of other countries.
- ZERVIATE®, indicated for the treatment of ocular itching associated with allergic conjunctivitis, has been exclusively licensed in the U.S. to U.S. partner Eyevance Pharmaceuticals, a subsidiary of Santen Pharmaceutical Co., Ltd. Nicox's exclusive Chinese partner, Ocumension Therapeutics, for the development and commercialization of ZERVIATE in China and the majority of Southeast Asian countries, has completed a phase 3 clinical study in China for ZERVIATE and is in the process of filing for marketing authorization in China. ZERVIATE is also subject to exclusive licensing agreements for its development and commercialization in other territories.

All figures have been rounded off to the nearest thousand, except if indicated otherwise.

The entities making up the Group at December 31, 2022 are presented in Note 28.

2. ACCOUNTING POLICIES

2.1. Basis of presentation and compliance statement

The consolidated financial statements were prepared in accordance with IFRS (International Financial Reporting Standards) and the IFRSs adopted by the European Union on December 31, 2022. The comparative figures are those of December 31, 2021.

The Company's Board of Directors adopted the consolidated financial statements on March 15, 2023. These financial statements will be submitted for approval to the shareholders' general meeting.

The Group has prepared its financial statements using the going concern basis of accounting. The Group currently estimates that it has sufficient cash to sustain its operations and thus ensure continuity of business over the next twelve months (see Note 25.4)

2.2. New standards, interpretations and amendments

The following standards, amendments and interpretations endorsed by the European Union became mandatory at December 31, 2022 but had no material impact on the Group's financial statements.

- Amendments to IAS 1 - Classification of liabilities as current or non-current;
- Amendments to IFRS 3, Business combinations ;
- Amendments to IAS 16 – Property, plant and equipment – Proceed before intended use;
- Amendments to IAS 37, Onerous contracts;
- 2018-2020 annual improvement cycle.

2.3. Standards, amendments and interpretations issued, but not yet in effect

2.3.1. *IFRS standards and amendments published but not yet eligible for adoption*

The following standards, amendments and interpretations have been published by the IASB but have not yet been adopted by the European Union or were not yet applicable at December 31, 2022. The potential impact of these standards on the statements of net profit or loss, the financial position or cash flows is currently being assessed by the Group.

- Amendments to IAS 1 - Presentation of Financial Statements; classification of debt with covenants
- Amendments to IAS 8 - Accounting policies, changes in accounting estimates and errors;
- Amendment to IFRS 16 - Lease liability in a sale and leaseback;
- IFRS 17 – Insurance contracts;
- Amendment to IAS 12 - Income taxes.

3. MAIN ACCOUNTING POLICIES

The Group applied the following accounting policies consistently to all periods presented in these consolidated financial statements.

3.1. Consolidation principles

3.1.1. *Subsidiaries*

Subsidiaries are entities over which the Group exercises control. The Group controls a subsidiary when it is exposed, or has rights, to variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity and is able to influence these returns due to the power it holds over this entity with regard to determining financial and operational policies. The financial statements of subsidiaries are included in the consolidated financial statements from the date on which control is obtained, and until the date on which control ceases. As wholly-owned companies, the Group controls all of the legal entities included in the scope of consolidation.

3.1.2. *Loss of control*

When the Group loses control of a subsidiary, it derecognizes the assets and liabilities as well as any non-controlling interests and other comprehensive income /loss items likely to be reclassified to income. Any gain or loss incurred from the loss of control is recognized under profit or loss. Any interest retained in the previous subsidiary is measured at fair value at the date that control is lost.

3.1.3. *Transactions eliminated on consolidation*

All significant intercompany balances and transactions are eliminated.

3.2. Business combinations

Any excess of the consideration transferred over the Group's share in the net fair value of identifiable assets and liabilities of the acquiree is recorded as goodwill.

In accordance with IAS 36 – *Impairment of assets*, goodwill is measured at cost, less accumulated impairment losses.

Goodwill is tested for impairment at least once a year for each of the Group's Cash Generating Units (CGU), and each time that events or circumstances indicate a potential impairment. These events or circumstances imply significant changes that are likely to have a long-term impact on the substance of the original investment.

Goodwill arising from the acquisition of foreign entities is measured in the acquired entity's operating currency and converted into euros using the exchange rate in effect at the end of the period.

3.3. Investments and other assets

Financial assets include investments and assets representing notes receivables from non-consolidated companies.

Non-consolidated shares and shares not listed on an active market are measured at fair value through profit or loss.

Financial assets representing a debt security are measured at amortized cost.

The financial interests of assets representing a debt security are calculated according to the effective interest rate method and credited to the "financial income" line item in the statement of profit or loss.

3.4. Foreign currency transactions and translation into Euros

The consolidated financial statements are presented in euros.

3.4.1. *Foreign currency transactions*

Foreign currency transactions are translated into the respective functional currencies of Group companies using the exchange rates prevailing at the dates of the transactions.

Assets and liabilities denominated in foreign currency are translated in the functional currency according to the exchange rate at the end of the period until settled. Exchange rate differences arising at the time of payment are recognized in the consolidated statement of profit or loss.

3.4.2. *Translation into euros*

Differences arise from translation into euros of all assets and liabilities and the income statement of consolidated entities prepared in another currency. Currency translation adjustments are recognized in the translation reserve included in other comprehensive income.

When a foreign asset is sold, either totally or partially, and there is a loss of control, the total amount of related currency translation adjustments must be reclassified in the statement of profit or loss as a disposal loss or gain. If the Group disposes of part of its interest in a subsidiary while retaining control, a proportion of the cumulative amount of the translation difference is reallocated to non-controlling interests.

3.5. Property, plant and equipment

Items of property, plant and equipment are measured at cost less accumulated depreciation and accumulated impairment losses. When significant components of an item of property, plant and equipment have different useful lives, they are accounted for as separate items (major components) of property, plant and equipment. Gains and losses on the disposal of property, plant and equipment are recognized in net income. Costs directly attributable to the acquisition are capitalized.

Subsequent expenditures are capitalized only when it is probable that future economic benefits associated with the expenditure will flow to the Group.

Depreciation is calculated so as to spread the cost of the asset less its residual value on a straight line basis over its estimated useful life. Leased assets recorded under IFRS 16 are depreciated over the shorter of the lease term and their useful lives unless the Group has reasonable assurance that it will obtain ownership at the end of the lease. Land is not depreciated.

Depreciation allowances are calculated on a straight line basis estimated according to the assets' useful lives.

The estimated useful lives of tangible assets for the current period and the comparative period are:

Laboratory equipment	8 years
Computer equipment	3-5 years
Company cars	3-5 years
Buildings	3-5 years
Office equipment and fixtures	5-10 years
Furniture	9-10 years

Depreciation methods, useful life and residual values are reviewed at each reporting date and adjusted if necessary.

3.6. Intangible assets

3.6.1. *Research and development*

3.6.1.1 *Research and development activities generated internally*

The Group does not capitalize internally generated development costs. In fact, considering the risks and uncertainties related to regulatory authorizations and to the research and development process, they reputedly do not meet the six criteria for capitalization (established by IAS 38 – *Intangible assets*) before

authorization is received to place the drugs on the market. As a result, these internally generated costs prior to obtaining marketing authorization - primarily costs for clinical studies - are generally recognized directly in expenses as research and development expenditures when incurred.

The Group subcontracts its research and development activities to outside partners. It recognizes expenses based on a percentage of work actually completed.

3.6.1.2 *Research and development activities acquired separately*

Payments for research and development activities acquired separately are capitalized in the "Research and development activities acquired separately" line item provided that they correspond to the definition of an intangible asset: a resource that is (i) controlled by the Group, (ii) supposed to generate future economic benefits for the Group and (iii) identifiable (i.e. is separate or stemming from contractual or legal rights). In accordance with the provisions of IAS 38.25, the first condition of capitalization (the probability that the entity will receive future economic benefits from the asset) is considered met for research and development activities acquired separately. Considering that the amount of payments is ascertainable, the second condition for capitalization (that cost can be accurately measured) has also been met. In consequence, the upfront payment and tiered payments to third parties for pharmaceutical products that have not yet received a marketing authorization are capitalized under intangible assets and amortized on a straight-line basis over their useful lives, up until the date this authorization is obtained. Research and development activities acquired separately by the Group were to be paid by means of contingent consideration and on that basis, were not capitalized, as they could not be reliably measured at the time of acquisition.

3.6.2. *Other intangible assets acquired as part of a business combination*

Other intangible assets acquired as part of a business combination relating to research and development projects in progress and to drugs currently being marketed, and which can be accurately measured, are identified separately from goodwill, measured at fair value and capitalized in *Other intangible assets*, in accordance with IFRS 3 – *Business combinations* and with IAS 38 – *Intangible assets*. A corresponding deferred tax liability is also recognized if a deductible or taxable temporary difference exists.

Research and development projects in progress acquired through a business combination are amortized on a straight-line basis over their estimated useful life starting from the date that the marketing authorization is obtained provided that the development of the asset has been fully completed. In the case of additional developments after market approval has been obtained which are necessary for completing the development of the asset, the commencement of amortization corresponds to this date of completion.

The rights for drugs marketed by the Group are amortized on a straight-line basis over their useful lives. These are determined by taking into account, among other factors, the corresponding legal period of patent protection. In June 2019, having completed the development of the asset in the US territory, the Group began to amortize the value of ZERVIATE associated with for those rights concerning the US territory but in response to developments in the US market for anti-allergy topicals, this asset was amortized in 2021.

3.6.3. *Research and development activities acquired separately*

Payments for research and development activities acquired separately are capitalized in the "Research and development activities acquired separately" line item provided that they correspond to the definition of an intangible asset: a resource that is (i) controlled by the Group, (ii) supposed to generate future economic benefits for the Group and (iii) identifiable (i.e. is separate or stemming from contractual or legal rights). In accordance with the provisions of IAS 38.25, the first condition of capitalization (the probability that the entity will receive future economic benefits from the asset) is considered met for research and development activities acquired separately. Considering that the amount of payments is ascertainable, the second condition for capitalization (that cost can be accurately measured) has also been met. In consequence, the upfront payment and tiered payments to third parties for pharmaceutical products that have not yet received a marketing authorization are capitalized under intangible assets and amortized on a straight-line basis over their useful lives, up until the date this authorization is obtained.

Research and development activities acquired separately by the Group were to be paid by means of contingent consideration and on that basis, were not capitalized, as they could not be reliably measured at the time of acquisition.

3.6.4. *Other intangible assets*

Other intangible assets acquired by the Group and with a finite useful life, including patents, are stated at cost less accumulated depreciation and accumulated impairment losses.

Intangible assets are amortized over their estimated useful lives.

Estimated useful lives for the current period and the comparative period are:

Computer software	3-5 years
Patents	Until the patent expiry date

Amortization methods and useful lives are reviewed at each closing date, and adjusted if necessary.

3.7. Impairment tests

Impairment tests are conducted on intangible assets as soon as evidence of impairment is identified. Intangible assets in progress, indefinite lived intangible assets and goodwill are tested at least once a year in the fourth quarter.

For impairment tests of goodwill, the Group has defined a single CGU relating to its pharmaceutical research and development activities. Following the Group's reorganization pursuant to the disposal of its European commercial operations, the Group has refocused its activities on research and development of international products. For that reason, the Group now has only one operating segment and therefore one GCU in light of the global nature of the R&D projects under development.

The methodology used primarily consists of comparing the recoverable amount of the Group’s CGU to the corresponding net asset (including goodwill).

The recoverable amount is the higher of fair value less costs to sell and its value in use. Value in use is determined using discounted future operating cash flows requiring the use of assumptions, estimates or assessments. Estimations of future operating cash flows are based on a medium-term strategic plan, the extrapolation of cash flows for the period after the medium-term strategic plan and a terminal value.

Additional impairment tests are performed if particular circumstances or events indicate a potential impairment. A sensitivity analysis of the impairment tests is presented in Note 9 and 10. Goodwill impairment is irreversible.

The value of non-current assets is evaluated at each closing date to determine if evidence of impairment exists. If evidence of a non-current asset’s impairment exists, the Group estimates the asset’s recoverable value. If the non-current asset’s carrying value exceeds its recoverable value, the asset is considered as impaired and its carrying value is written down to its recoverable value.

3.8. Other financial assets

3.8.1. Trade receivables

Trade and other receivables are measured at fair value, which is the nominal value of invoices unless payment terms require a material adjustment for the time value discounting effect at market interest rates. A valuation allowance for trade receivables is recognized if their recoverable amount is less than their carrying amount.

3.8.2. Cash and cash equivalents

Short-term cash deposits listed in the statement of financial position include cash at bank and in hand, as well as short-term deposits with initial maturities of less than three months subject to an insignificant risk of changes in value and items which can be settled immediately without any significant penalty.

3.8.3. Government grants receivable

The research tax credit is granted to companies by the French tax authorities as an incentive measure to conduct technical and scientific research. Companies able to demonstrate that they incur research expenses meeting the criteria of the research tax credit qualify for a tax credit that may be used for the payment of their corporate income tax for the period in which these expenses were incurred, and for the three following financial years. If the taxes payable do not cover the total amount of the tax credit at the end of this three-year period, the Group receives a cash refund by the tax authorities for the difference. The Group also meets the criteria of the definition for small and medium-size companies, and on that basis may request an immediate payment of this tax credit. Only expenses devoted to research are included in the calculation for the research tax credit (RTC).

The Group concluded that the RTC met the definition of a government grant according to the definition listed under IAS 20 – *Accounting for government grants and disclosure of government assistance*, and it was recognized as other income within operating income on the statement of profit or loss.

3.9. Share-based payments

The Group awards its employees, including senior executives, with share-based compensation (stock options and restricted stock units). Some non-employees (consultants, members of the glaucoma clinical advisory board) included within the IFRS 2 – *Share-based payments* definition of "employees and others providing similar services" also receive compensation paid in equity instruments (equity warrants) in return for their services to the Group.

All new awards active to date have been subject to performance conditions making the final allocation of share-based payments uncertain until the performance criteria are met. Accordingly, the fair value of services received, including the estimate of the number of awards that will vest based on the probability of meeting the performance conditions, is evaluated at each reporting date until final allocation of the share-based payments. For stock options, the valuation results are calculated using the Black-Scholes formula. The expected long-term volatility was determined on the basis of Company's average historical volatility. Based on Group forecasts, no dividend payments are anticipated in the coming years. The fair value of equity warrants granted to members of the glaucoma clinical advisory board is estimated at the grant date using the Black-Scholes formula.

The cost of equity-settled transactions is recognized in expenses with a corresponding entry in equity over the vesting period. This period ends on the date when the rights to compensation are fully vested. The cumulative expense recognized for these transactions at each reporting date until the vesting date reflects the vesting period and the number of shares that will eventually vest. The estimated expense is revised if later information indicates that the number of shares expected to be vested differs from a previous estimation.

If recipients of equity-settled share-based payments leave the Group prior to the vesting of the awards, in the absence of a decision to the contrary by the Board of Directors, they do not acquire the rights providing access to the corresponding equity instruments granted to them, and consequently, no expense is recorded. However, if the beneficiary ceases work with the Group after the vesting period, or continues to work with the group without exercising his/her rights, the previously recognized expense will not be reversed.

3.10. Buyback of common shares (treasury shares) and their release back into circulation

The Group implemented a share buyback program authorized by the ordinary general meeting of June 16, 2020 for the purpose of maintaining an orderly market for the liquidity of the Nicox share by an investment

service provider within the framework of a liquidity agreement. If the Group buys back its own equity instruments, the amount of consideration paid, including directly attributable costs, is recognized as a decrease in equity. The shares bought back are classified as treasury shares in the treasury share reserve. When treasury shares are sold or released back into circulation, the amount received is recognized as an increase in equity, and the positive or negative balance from the transaction is presented in reserves.

3.11. Provisions and contingent consideration in a business combination

A provision is recognized when the Group has a legal or constructive obligation towards a third party as a result of a past event and it is probable that it will result in an outflow or resources embodying economic benefits without receipt of equivalent consideration and a reliable estimate of the amount of the obligation cannot be made. The amount of a provision represents the best estimate of the expenditure required to settle the obligation at the reporting date. To determine the present value of the obligation the discount rate applied is a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the liability. Increases in a provision reflecting the passage of time are recorded under interest expense.

Except for contingent liabilities linked to business combinations, as well as asset acquisitions, contingent liabilities are not recognized, but are presented in the notes to the financial statements, unless the likelihood of a cash outflow is very low.

Contingent consideration is recognized under equity when payment of the consideration is settled by a fixed number of equity instruments and in other cases under financial liabilities linked to business combinations. Contingent considerations linked to a business combination is measured at fair value at the time of the business combination regardless of the degree of probability of an inflow or outflow of economic benefits. If the contingent consideration on initial recognition is recorded as a financial liability, subsequent adjustments to liabilities are recognized in the consolidated statement of profit or loss under "Fair value adjustment of contingent consideration".

3.12. Post-employment obligations

The Group's commitments under defined benefit retirement plans are determined using the projected unit credit actuarial cost method. These plans are unfunded. These obligations are measured at the end of each reporting period. The actuarial assumptions used to determine these obligations take into account the prevailing economic conditions in the relevant country. The Group's commitments are recorded as liabilities. Any actuarial differences are recognized in other comprehensive income for the fiscal year.

3.13. Revenue

Revenue of the Group is derived from the licensing of drug candidates that have received a marketing authorization or licensed to partners responsible for their development.

Royalties received as consideration for product sales licensed to partners are recognized under revenue when sales are completed. The Group recognizes revenue generated from these licenses of intellectual property in accordance with IFRS 15.

For this purpose, the Group determines if the license granted represents a right to access or a right to use the intellectual property. This, along with other terms and conditions related to payments made, makes it possible to determine the appropriate revenue recognition method for the different milestones, including any up-front payments, provided for in the contract.

Revenue derived from milestones based on objectives for sales levels or royalties based on sales is recognized when the objectives for sales levels or sales on which the royalties are based are realized in connection with the license.

Revenue resulting from variable consideration is recognized only to the extent that it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

3.14. Leasing and subleasing contracts

A lessee recognizes a right to use an asset (right-of-use asset) and a financial liability (lease liability). The right-of-use asset is not recognized under a separate line but instead in the line corresponding to the underlying asset. The right-of-use asset is amortized over the expected term of the lease and the lease liability, is initially recognized at the present value of lease payments over the lease term using the interest rate implicit in the lease when this can be readily determined or, otherwise, at the incremental borrowing rate.

In the statement of profit or loss, the depreciation of the right-of-use asset is included in the operating profit or loss before the amortization of intangible assets and a finance expense corresponding to interests on the lease liability is recognized under finance expenses.

In the statement of cash flows, interest expenses are allocated to cash flows used in operating activities and the repayment of lease liabilities is allocated to cash flows used in investing activities.

At the end of July 2022, a sublease agreement for the premises of the Nicox Ophthalmics subsidiary was signed with Goodwill Industries.
This contract was classified as a finance lease on the basis of the right of use resulting from the main lease contract.
At December 31, 2022, the right of use under the master lease was derecognized, and a receivable was recognized for an amount equal to the net investment in the sub-lease, with the difference between the right of use and the net investment in the lease recognized in profit or loss, while the lease liability (under the master lease) was maintained under liabilities.

3.15. Income tax

Income tax expense comprises current and deferred taxes. It is recognized under net income unless it related to items recognized directly in equity or other comprehensive income.

Current tax includes the estimated amount of tax payable (or receivable) for taxable profit (or loss) of a period or any adjustment to the amount of tax payable in respect of previous periods. It is calculated at the tax rates that have been enacted or substantively enacted by the balance sheet date.

Current tax assets and liabilities are offset if certain criteria are met.

Deferred taxes are calculated based on temporary differences existing between the book value and the tax value of the assets and liabilities. The following items do not give rise to the recognition of deferred tax:

- Temporary differences arising from initial recognition of an asset or liability in a transaction that is not a business combination and that affects neither accounting profit nor the taxable profit; and

- Temporary differences arising from investments in subsidiaries, associates and partnerships to the extent that the Group is able to control the timing of the reversal of these differences and it is probable that the reversal will not occur in the foreseeable future.

Deferred tax liabilities are recognized for all temporary differences between the book value and the tax value of the assets and liabilities acquired through business combinations.

Deferred tax assets are recognized for tax losses, unused tax losses, unused income tax credits and deductible temporary differences when it is probable that future taxable income will be available against which the deductible temporary differences can be utilized for the Group. The deferred tax assets are evaluated at the end of each reporting period and are not recognized when the availability of a sufficient tax profit becomes improbable.

Unrecognized deferred tax assets are remeasured at each balance sheet date and recognized when there is a strong likelihood that sufficient future taxable profits will be available against which the unused losses can be utilized.

Deferred tax is calculated at the tax rates that are expected to apply on the temporary differences when they are reversed, based on tax rates that have been adopted or substantively adopted as of the balance sheet date.

The measurement of deferred taxes should reflect the tax consequences that would follow from the manner in which the Group expects, at the balance sheet date, to recover or settle the carrying amount of its assets and liabilities.

Deferred tax assets and liabilities are offset provided that certain criteria are met.

3.16. Financial liabilities recognized at amortized cost

Borrowings and other financial liabilities are initially recognized at fair value less directly attributable transaction costs and subsequently at amortized cost calculated using the effective interest rate. The portion of financial liabilities of less than one year is presented under “current financial liabilities.

Because the Kreos debt restructuring in 2021 was considered substantial as defined by IFRS 9, the debt was deemed to have been extinguished in exchange for the issuance of three new debt issues recognized at their fair value at the date of the restructuring. The difference between the net book value of the extinguished debt and the fair value of the new debt issues was recognized under finance expense in the statement of profit and loss. All fees and commissions incurred on this transaction were recorded directly in the statement of profit and loss under administrative expenses.

The convertible bond is considered as hybrid financial instrument combining a bond component recorded under debt at fair value and an equity component. This conversion option, which meets the definition of an equity instrument under IAS 32, was recognized under equity. The debt component of the convertible bond was recognized on the renegotiation date at fair value (see Note 20).

3.17. Financial liabilities resulting in the repurchase of equity instruments

In connection with the issue of ordinary shares with warrants (ABSA) in November 2022 in the amount of €10 million to a single subscriber, Armistice Capital, the Company granted Armistice Capital a "Put Option" pursuant to which the Company has contractually undertaken, subject to certain conditions, to repurchase the warrants from Armistice Capital (see Note 4.7).

This "Put Option" was contractually concluded between the Company and Armistice Capital separately from the warrants. As a result, should the warrants be transferred to another holder, the right to request their repurchase would not be transferred to the holder. In accordance with IAS 32, the warrants are considered as equity instruments.

The sale of the "Put Option" to the subscriber is recognized under IAS 32 as a financial instrument (separately from the warrants) which could require the Company to repurchase its own equity instruments (in this case the warrants) in return for cash consideration.

In accordance with IAS 32.23, this option granted to the subscriber creates a financial liability for the Company equivalent to the present value of the repurchase amount (see Note 20). On the issue date, the

redemption value of the warrants under the "Put Option" was recognized under financial liabilities with a corresponding entry under shareholders' equity. This debt is subsequently measured in accordance with IFRS 9 and any subsequent remeasurement of its redemption value is recognized under profit or loss (see Note 5.7.2). If the put option expires without the warrants' redemption, the carrying value of the financial liability at that date will be reclassified directly under equity.

3.18. Subsequent events

The consolidated financial statements are adjusted to reflect subsequent events that alter the amounts relating to conditions existing at the date of the statement of financial position. The adjustments are made up to the date of approval of the financial statements by the Board of Directors. Other events subsequent to the closing date that do not result in adjustments are presented in Note 30.

4. CRITICAL ACCOUNTING ESTIMATES AND ASSUMPTIONS

In preparing the consolidated financial statements, the Group's management has to make certain judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts recognized in the financial statements.

The underlying estimates and assumptions are reviewed on an ongoing basis. Changes in these estimates are accounted for prospectively. Information on the use of estimates, assumptions and judgments in connection with the application of accounting policies with the most significant impact on amounts recognized in the consolidated financial statements are presented below.

4.1. Fair value of financial instruments

In accordance with IFRS 13 and IFRS 7, the fair value measurements of these financial instruments must be classified according to a hierarchy according to inputs used to measure the instrument at fair value. This fair value hierarchy is comprised of the following levels:

- level 1: use of quoted prices on active markets (unadjusted) for identical assets or liabilities that the company can assess on the measurement date;
- level 2: use of quoted prices on active markets for similar assets or liabilities or derived from all significant inputs that are corroborated by observable market data (market-corroborated inputs); and
- level 3: use of valuation techniques for which significant inputs are not all based on significant observable market data.

The table below presents the disclosures required by IFRS 7 on the valuation principles for financial instruments.

Nature of the financial instrument	Valuation principle	Fair value level	Valuation model
Negotiable debt securities, commercial paper, demand deposits and term deposits	Amortized cost	n/a	For instruments with a maturity of less than three months, amortized cost is an acceptable approximation of fair value as disclosed in the notes to the consolidated financial statements

Financial liabilities	Amortized cost	n/a	The fair value indicated in the notes to the consolidated financial statements is determined according to the present value of residual cash flows based on observable market data at that date.
Put option	Present value	n/a	The financial liability (corresponding to the Put Option) on initial recognition must be measured at the present value of the repurchase amount with an offset under equity. This value is determined by discounting a Black and Sholes calculation based on the share price at year-end and contractually predefined minimum volatility of the Nicox share.
Lease liabilities	Amortized cost	n/a	Future lease liabilities are discounted using the incremental borrowing rate;

4.2. Licensing agreements granted

In December 2018,the Group entered into an exclusive license agreement with Ocumension Therapeutics, an international ophthalmology company. The agreement concerns the development and commercialization of its NCX 470 drug candidate, targeting patients with glaucoma or ocular hypertension for a territory comprising mainland China, Hong Kong, Macau, and Taiwan. Ocumension received exclusive rights to develop and commercialize NCX 470, at its own costs, in the agreed territory. Under the terms of the agreement, Nicox received in December 2018 a one-time upfront payment of €3 million from Ocumension and was also eligible to receive up to an additional €14.5 million in milestones associated with Ocumension's progress with NCX 470, up to and including regulatory approval, and up to €16.25 million associated with potential sales in the territory, as well as tiered royalties from 6% to 12% on sales.

In March 2020, Nicox signed an amendment to the license agreement with Ocumension for NCX 470. Under the amended agreement, Ocumension paid Nicox €15 million (of which €14 million is repayable under certain conditions), replacing in full the milestone payments under the original agreement. Under the amended agreement, Ocumension gained additional exclusive rights to NCX 470 for South Korea and South East Asia and undertakes to pay 50% of the costs of the second glaucoma Phase 3 clinical trial of NCX 470 ("Denali"). The two companies jointly manage the Denali trial in the U.S. and China. No future NCX 470 milestones will be due from Ocumension to Nicox. In the unlikely case that the Joint Trial would not take place, partial refunds may be made and in certain situations the original milestones of the agreement would again apply. The tiered royalties of 6% to 12% of the original agreement remain unchanged and will apply to sales in the original and the additional territories.

The Group has considered that there were no new performance obligations in connection with the signature of this amendment and that €1 million could be immediately recognized under revenue. A residual amount of €14 million (initially recorded under deferred revenue) will be recognized as revenue only if it becomes highly probable that the uncertainty associated with the variable consideration is subsequently resolved and the potential repayment clauses shall not result in an adjustment involving a significant decrease in the cumulative amount of revenue recognized. Out of the €14 million initially recognized as deferred revenue, €1.5 million at December 31, 2022 will be recognized only if it is highly probable that the uncertainty associated with the potential repayment clauses do not result in an adjustment involving a significant decrease in the cumulative amount of revenue recognized. No revenue was recognized for this contract in 2022, compared with €3 million for the 2021 full-year.

In the Group's view, the joint Phase 3 clinical trial ("Denali") enters into the scope of IFRS 11 on "Joint arrangements" and in consequence expenses relating to this trial will be recognized in the consolidated statement of profit or loss as incurred.

In July 2021, the Group also amended its license agreement with Ocumension, under which the latter is granted exclusive rights to develop and commercialize ZERVIATE® (cetirizine ophthalmic solution), 0.24% in the Chinese and the majority of Southeast Asian markets. Under this amended agreement, Ocumension immediately paid Nicox US$2 million in full advance payment of the future development and regulatory milestones for the ZERVIATE®. This US$2 million was fully recognized under revenue during 2021.

The other license agreements not requiring determinant estimates and accounting judgments for fiscal 2022 are described in Note 23.1.

4.3. Financing provided by Kreos

Nicox entered into a financing agreement for up to €20 million with Kreos Capital, structured as senior secured bonds in three tranches, which were disbursed between February 1, 2019 and January 2, 2020. In January 2021, Nicox amended its bond financing agreement with Kreos Capital, introducing an additional one-year period of interest-only payments on the outstanding principal starting on February 1, 2021, and extending the overall period of the loan by 6 months to July 2024. This extension applied to all three tranches of the loan amount and provided for repayment according to the same payment schedule.

On November 30, 2021, a new amendment to the bond financing agreement was introduced. At that date, the outstanding principal amount was €16.9 million, which included a prepayment of €0.6 million upon the call of the tranches. These €0.6 million amounts correspond to the final payments of the principal for each of the tranches called. Under this amendment, the interest-only period was increased by 18 months to July 2023 (against January 2022 previously) and the maturity date of the loan was increased by 18 months to 1 January 2026. In addition, this amendment introduced an option to further extend the interest-only period and the maturity date by 6 additional months if the Mont Blanc Phase 3 NCX 470 clinical trial meets the primary endpoint of non-inferiority compared to latanoprost. These changes applied to 70% of the outstanding principal, excluding pre-payments of €0.6 million (the "Term Loan"). The 9.25% interest rate remains unchanged. In exchange for extending the repayment period by an additional 18 months of interest-only payments on the "Term Loan", €3.3 million of the outstanding principal amount prior to the amendment was issued in the form of convertible bonds (the "Convertible Loan"). The term will be 1 January 2026 with the same interest rate of 9.25% per annum, payable in cash. The Convertible Loan will be secured against the collateral in place for the Term Loan. This portion of the debt can be converted into shares at Kreos' discretion at any time (after an initial 60-day period) up to the maturity date of 1 January 2026. The conversion price was €3.67. If Kreos has not converted the Convertible Loan by the end of the repayment period of the Term Loan, the entire amount of the Convertible Loan remaining is due as a single payment at that time. Should Kreos convert the bonds, the participation of existing shareholders in the Company's share capital would be diluted. The interest rate of 9.25% will remain unchanged and interest will be payable until maturity on January 1, 2026.

The remaining €1.8 million was issued in the form of new non-convertible bonds with an interest rate of 9.25% and the same term as the Convertible Loan and with an additional premium payable at repayment such that the total return to Kreos is 1.75 times the original amount. The interest rate of 9.25% remains unchanged and interest is payable until maturity on January 1, 2026.

Following its restructuring, this bond financing arrangement is now divided into three parts:

- Convertible bonds with a nominal amount of €3,300,000,
- Non-convertible bonds for a nominal amount of €11,870,000,
- Non-convertible bonds with a repayment premium for a nominal amount of €1,787,000.

Because the restructuring of the bond financing agreement is considered substantial in accordance with IFRS 9, the Kreos bond financing debt amounting to a total nominal amount of €16,958,000 was considered extinguished in exchange for three new bond issues recognized at fair value at the restructuring date.

The difference between the net book value of the extinguished debt and the fair value of the new debt issues was recognized under finance expense in the statement of profit and loss in the amount of €2,962,000. All fees and commissions incurred on this transaction were recorded directly in the statement of profit and loss under administrative expenses in the amount of €355,000. These different transactions were recognized in 2021. The convertible bond is considered as hybrid financial instrument combining a bond component recorded under debt at fair value and an equity component. This conversion option, which meets the definition of an equity instrument under IAS 32, was recognized under equity in the amount of €635,000 (before deferred tax liabilities). The debt component of the convertible bond was recognized on the renegotiation date at fair value for a total amount of €3,268,000.

After initial recognition, bonds recognized under financial liabilities are measured at amortized cost. The carrying amount of these bonds recognized as financial liabilities was €18,700,000 as of December 31, 2022.

The contract provides for various events of default, and in particular a breach of a material obligation of the contract, such as payment of amounts due or failure to provide financial information; failure to pay a debt exceeding €150,000; initiation of legal proceedings or suspension of activity; change of control (in case of exercise of the put option). In the case of an event of default under the agreement, the amounts due under the loan would become immediately repayable and, in the event of non-payment, Kreos could enforce the security guarantees. There can be no assurance that Nicox will have the resources required for the early repayment of this bond issue.

The Company has granted security interests in certain of its tangible and intangible assets, including patents relating to the VYZULTA product (the pledge having no impact on the exclusive worldwide license agreement with Bausch + Lomb), the securities of the subsidiary, Nicox Ophthalmics Inc., as well as a pledge of bank account balances and Risks associated with income and exchange rate fluctuations, reliability of investments.

In November 2022, the Company exercised the option to extend the interest-only payment period and the maturity date of the loan for an additional 6 months to January 2024 and July 2026, respectively, as the Mont Blanc Phase 3 clinical trial for NCX 470 met its primary endpoint of non-inferiority to latanoprost before July[1,] 2023. This extension does not apply to the convertible bonds with a nominal amount of €3.3 million or the non-convertible bonds with a nominal amount of €1.8 million, for which the maturity date, including premium, remains January 1, 2026.

This extension has deferred repayment of the principal due for the period from August 1, 2023 to January 1, 2024 in the amount of €2.1 million. On that basis, the repayment will be made from February 2024 to July 2026. This option to extend the loan by a further six months resulted in an additional interest payment of €0.8 million in 2026.

4.4 Company objectives

The Board of Directors sets the Group's objectives each year. Achieving these objectives is one of the criteria upon which variable compensation is calculated for certain employees. Furthermore, Group employees receive share-based compensation (stock options and restricted stock units). The vesting of this share-based compensation is subject to performance conditions requiring that at least 50% of the Group's yearly objectives set by the Board of Directors are met for the calendar year concerned. In the event that these performance conditions are not met, half of the rights granted for 2022 (i.e. 50% + 1 option) will be definitively canceled, with the other half of the rights remaining in effect for the stock options and restricted stock units. The performance of the 2022 objectives was measured by the Board of Directors at 100% which is in line with the amount of the expense recognized.

4.5 Economic context

The Group closely monitors the situation and apprises the market if there is any impact, notably on its development programs, its financing needs or revenues. The Group has not identified any indications of impairment which might result in the recognition of an impairment loss for its intangible assets, including goodwill due to the pandemic. However, the Group is experiencing delays in the clinical enrollment of patients in the Denali study due to both the ongoing impact of COVID-19 in China, where 20% of patients were expected to be enrolled, and a longer term impact on the glaucoma clinical trial environment from the pandemic period.

With respect to its cash position, the Group obtained loan agreements guaranteed by the French State with Société Générale and LCL for a total amount of €2 million under measures made available under COVID-19 relief measures. These loans are not secured against any of the Group's assets. Up to 90% of the loan is guaranteed by the French State (interest-free during this period). It has an initial maturity of 12 months which may be extended for an additional year and with the option for Nicox to take a 1 to 5-year repayment period after that. In addition, in November 2022, the Group raised €10 million in gross proceeds and restructured its loan agreement with Kreos, thus ensuring a cash flow runway until mid-June 2024. The COVID-19 pandemic has had an impact on the progress of the Group's development programs within the established timetables, notably the Phase 3 Denali study on NCX470, and particularly on the Chinese part of this study. Should the COVID-19 pandemic, or any other comparable health situation, once again impact the development of the NCX 470 program, this could have a significant negative effect on the Group, its business, financial situation and results, as well as on its development and prospects.

No direct future impact on the Group's financial position has been identified as a consequence of the Russia/Ukraine conflict, which began in February 2022. As of the date of this document, the Group has no customers in these regions and no plans to develop significant business activity there in the short or medium term. The Group also has no direct exposure in the area of research and development. Despite however the fact that this conflict has no significant impact on the Group's performance, it remains unable at this stage to predict the macroeconomic consequences of this geopolitical situation and its evolution on its future performance.

4.6 Impairment of intangible assets

In February 2022, Nicox announced that it will be focusing the future development of NCX 4251 on dry eye disease rather than the indication for blepharitis as initially planned. This decision follows the post hoc results from the Mississippi Phase 2b clinical trial and a subsequent meeting with the U.S. Food and Drug Administration (FDA). Nicox completely revised its development plan for NCX 4251, which has led to an impairment of this asset in December 2021 in the amount of US$17,846,000. This impairment reflects mainly an increase in development costs, the time required to complete the studies and bring the product to market as well as a higher percentage of success in future clinical trials. On June 30, 2022, the Group decided to seek a partner to pursue the product's development outside China where it is licensed to Ocumension Therapeutics and as a consequence recognized an additional impairment charge of US$11,456,000. The net book value of NCX 4251 after impairment now stands at US$3,698,000 (€3,467,000), which is the value in use for this asset and limited to the Chinese territory for which the rights have been licensed to Ocumension. The impairment of the period was recognized in the consolidated statement of profit or loss under "*Impairment of intangible assets*".

4.7 Put option on warrants issued in connection with the private placement in November 2022

Issuance of shares with warrants attached (ABSAs)

In November 2022, the Group carried out a capital increase without preferential subscription rights through the issuance of 6,849,316 new ordinary shares, each with a warrant attached conferring a right to subscribe to an additional 6,849,316 new ordinary shares for a period of five years following the allotment of the warrants. The subscription was reserved to one or more companies or collective investment funds, governed by French or foreign law, or natural persons habitually investing in the pharmaceutical/biotechnology sector. This issue was subscribed by a single investor, Armistice Capital.

The exercise price or the warrants set by the Board of Directors on November 21, 2022 was €1.70.

The characteristics of the ordinary shares and warrants issued meet the definition of an equity instrument under IAS 32 and the amount of the issue of shares with warrants attached (i.e. €10 million) was recognized directly in equity.

Issuance of a put option on the warrants (maturity November 2027)

As part of the private placement of the shares with warrants attached, the Company granted Armistice Capital a "**Put Option**" whereby NICOX contractually undertook, subject to certain conditions, to repurchase the warrants from Armistice Capital. The contractual characteristics of this BSA put option are as follows: Should the Company be subject, during the period in which the warrants resulting from the capital increase are outstanding, to a merger by absorption or by the creation of a new company control, a spinoff or a change in control within the meaning of article L. 233-3 I of the French Commercial Code, for which the consideration would consist in the delivery of securities whose exchange ratio would result in a value per share lower than the exercise price of the warrants, Armistice Capital, the holder of the warrants, may ask the Company (after the completion of the transaction) to repurchase its warrants at a price determined in accordance with a Black Scholes formula. The assumptions to be used for this Black Scholes calculation, including a minimum level of volatility, have been contractually defined. Should the warrants be transferred to another holder, the right to request their repurchase would not be transferred to this holder.

The sale of this option to Armistice Capital is recognized in accordance with IFRS as a financial instrument (separately from the warrants) which could require Nicox to repurchase its own equity instruments (in this case the warrants) in return for cash consideration. In accordance with IAS 32.23, this option granted to Armistice Capital creates a financial liability for Nicox equal to the present value of the repurchase amount. At the issue date, the repurchase value of the warrants under the "Put Option" was valued at €7.2 million and was recognized as a financial liability with a corresponding entry in shareholders' equity.

This debt is subsequently measured in accordance with IFRS 9 and any subsequent remeasurement of its redemption value is recognized under profit or loss. At December 31, 2022, the financial liability of the "Put Option" measured according to the evaluation model amounted to €4.1 million (see Note 20). The change in value between the issue date and December 31, 2022 of €3.1 million was recognized as income under "Net financial income (expense)" (see Note 5.9.2).

If the put option expires without the warrants' redemption, the carrying value of the financial liability at that date will be reclassified directly under equity.

5. INCOME AND EXPENSES

5.1. Segment information

In accordance with the definition of sectors drawn up according to IFRS 8 – Operating segments, the segment breakdown includes only a single segment reflecting the Group's operating and managerial structure which is focused on pharmaceutical research and development. In 2022 and 2021, all intangible assets were located in the United States, tangible assets mainly in the United States and non-current financial assets in Europe.

5.2. Revenue from collaborations

Revenue from collaborations breaks down as follows:

	For the year ended	
	2022	2021
	In €000	
Milestone payments	-	4,821
License royalty payments	5,242	3,762
Total revenue from collaborations	**5,242**	**8,583**

Revenue recognized in the year ended December 31, 2022 was derived exclusively from royalties on net sales of VYZULTA (licensed to Baush + Lomb) in the United States, Canada and in other countries. ZERVIATE (licensed to Eyevance) did not earn royalties in the United States due to a stockout in the first three quarters. And while the fourth quarter generated royalties, these were offset by the negative net sales of the previous quarters in accordance with contractual terms.

Revenue recognized in the year ended December 31, 2021 was derived largely from the amendments to license agreements with Ocumension for the NCX 470 and ZERVIATE drug candidates for China (see Note 4.2), or 56.2% of revenue for the period and royalties on net sales of VYZULTA in the United States and Canada and ZERVIATE in the United States licensed respectively to Baush + Lomb and Eyevance or 43.8% of sales for the period.

For additional information, see also Notes 4.2 and 23.1.

5.3. Royalty payments to PFIZER

Payment of royalties to PFIZER depends on revenues recognized with Bausch & Lomb. These payments constitute consideration for reacquiring the rights to latanoprostene bunod from Pfizer in 2009 in the form of a percentage of royalties on sales paid by Bausch & Lomb and part of a milestone payment received when the product obtained FDA approval. These payments amounted to €1,971,000 in 2022 compared to €1,350,000 in 2021.

5.4. Net profit from collaborations

Net profit from collaborations, defined as revenue from collaborations less royalty payments, amounted to €3,271,000 in 2022 compared to €7,233,000 one year earlier. The decrease in revenues from collaborations reflects the decline in royalties from sales of Vyzulta in the United States, licensed to Bausch & Lomb, and the absence of royalties from ZERVIATE, licensed to Eyevance. See Note 5.2

5.5. Research and development expenditures

On December 31, 2022 and 2021, research and development costs amounted to €17,992,000 and €17,910,000 respectively, breaking down by the nature and by projects in the table below as follows:

	For the year ended December 31	
	2022	2021
	In €000	
Internal expenditures	4,370	4,031
External expenditures	13,406	13,619
ZERVIATE (AC170)	63	100
NCX4251	496	3,918
*NCX470**	11,792	8,804
Other expenses not allocated by project	1,055	797
Other expenditures	217	260
Total R&D expenditures	**17,992**	**17,910**

* Net of expenses charged back to Ocumension relating to the Denali study (see Note 4.2)

Research and development expenditures remained stable in fiscal year 2022 despite the absence of development costs for NCX 4251 because of the increase in spending on Mont-Blanc clinical studies (completed in October 2022) and the continuation of Denali for NCX 470.

5.6. Administrative expenses.

General and administrative costs in 2022 and 2021 amounted to €7,479,000 and €7,000,000 respectively. General and administrative costs include mainly the cost of administrative and financial personnel, compensation to company officers, communications and business development costs. General and administrative costs also included in 2022 and 2021 respectively €717,000 and €661,000 for the measurement of stock options, restricted stock units and stock options awarded to Group employees and directors.

5.7. Other income

Other income in 2022 and 2021 amounted to respectively €762,000 and 843,000, breaking down as follows:

	For the year ended December 31	
	2022	2021
	In €000	
Research tax credit	504	716
Unrealized gains on assets and liabilities denominated in foreign currencies	258	53
Miscellaneous		74

Total	**762**	**843**

5.8. Other expenses

	For the year ended December 31	
	2022	2021
	In €000	
Reorganization expenses [(1)]	(1,459)	-
Unrealized foreign exchange losses	(256)	(205)
Other	(38)	(6)
Total	**(1,753)**	**(211)**

(1) Mainly separation payments to the former Chairman and Chief Executive Officer following the decision of the Board of Directors to terminate his appointment on June 1, 2022.

5.9. Expense by nature

Expenses by nature are presented below under the appropriate headings of the statement of profit or loss by function:

5.9.1. Personnel costs

	For the year ended December 31	
	2022	2021
	In €000	
Salaries (1)	(6,069)	(4,211)
Social charges	(1,767)	(1,562)
Pension expenses	(51)	67
Expenses related to share-based payments	(1,182)	(1,453)
Total personnel expenses	**(9,069)**	**(7,159)**

(1) Includes separation payments to the former Chairman and Chief Executive Officer following the decision of the Board of Directors to terminate his appointment on June 1, 2022.

5.9.2. Net financial income (expense)

	For the year ended December 31

	2022	2021
	In €000	
Foreign exchange gain	2,460	3,403
Capitalized interest on notes receivable (see Note 4.3)	-	-
Interest on cash equivalents	520	-
Change in fair value of the "Put Option" for warrants	3,039	
Other financial income	43	53
Total financial income	**6,062**	**3,456**
Foreign exchange loss	(146)	-
Financial interest paid on financial liabilities	(1,755)	(2,023)
Loss on the notes receivable and minority interests (see Note 4.3)	(11)	(2,814)
Other expenses	(376)	(14)
Total financial expenses	**(2,288)**	**(4,851)**
Net financial income (expense)	**3,774**	**(1,395)**

6. INCOME TAX

	For the year ended December 31	
	2022	2021
	In €000	
Current income tax (expense) / income [1]	30	(35)
Deferred tax (expense) / income (2)	2,498	3,679
Total tax (expense) income	**2,528**	**3,644**

(1) See Note 27.1.3
(2) See Note 21.

Reconciliation of the effective tax expense and applicable tax rate for the year ended

	For the year ended December 31	
	2022	2021
	In €000	
Loss before tax	(30,286)	(47,405)
Tax rate applicable to the Company	25%	26.50%
Theoretical tax loss carryforwards	7,572	12,562
Tax impact:		
From permanent differences	244	4,919
From share-based payments	(296)	(388)
From tax losses for which no deferred taxes have been recognized	(4,826)	(3,832)
Changes in estimates on the deferred tax bases		-
From other differences	(166)	221
Effective tax (expense) / benefit [1]	2,528	3,644
Effective tax rate	8.35%	7.69%

(1) Tax income for the years 2022 and 2021 reflects mainly the reversal of deferred tax liabilities following the impairment of intangible assets.

7. EARNINGS PER SHARE

7.1 Basic loss per share

Basic earnings per share are calculated by dividing net profit for the period attributable to ordinary equity holders of the parent by the weighted average number of ordinary shares outstanding during the financial year.

	For the year ended December 31	
	2022	2021
	In €000s (except share and per share items)	
Loss attributable to the ordinary equity holders	(27,759)	(43,761)
Weighted average number of ordinary shares outstanding	43,971,634	37,486,570
Basic loss per share	**(0.63)**	**(1.17)**

Diluted earnings per share are calculated by dividing net profit for the period attributable to ordinary equity holders of the parent by the weighted average number of ordinary shares outstanding adjusted for the effect of all potentially dilutive ordinary shares. For the years ended December 31, 2022 and 2021, the stock options, equity warrants and restricted stock units have no dilutive effect. As a result, the diluted loss per share equals the basic loss per share.

8. PROPERTY, PLANT AND EQUIPMENT

8.1 Breakdown by nature

	At December 31	
	2022	2021
	In €000	
Laboratory equipment	1,073	1,190
Computer equipment	511	478
Transportation equipment	146	122
Furniture	239	247
Fixtures and fittings	298	291
Buildings [(1)]	335	1,427
Gross value	**2,602**	**3,755**
Laboratory equipment	(1,071)	(1,187)
Computer equipment	(472)	(454)
Transportation equipment	(71)	(63)
Furniture	(237)	(236)
Fixtures and fittings	(284)	(277)
Buildings	(227)	(515)
Accumulated depreciation	**(2,362)**	**(2,732)**
Net value of property, plant and equipment	**240**	**1,023**

(1) Because the sublease granted to Goodwill Industries was classified as a finance lease, €1,236,000 capitalized under the original lease was reversed at December 31, 2022. See 3.14

8.2 Change in the year

	Gross value	Amortization and depreciation	Net value
		In €000	
Value at December 31, 2020	**3,810**	**(2,644)**	**1,166**
Acquisitions/Depreciation	228	(433)	(205)
Disposals or retirements	(381)	380	(1)
Impact of change in exchange rates	98	(35)	63
Value at December 31, 2021	**3,755**	**(2,732)**	**1,023**
Acquisitions/Depreciation	101	(333)	(232)
Disposals or retirements	(1,348)	741	(607)
Impact of change in exchange rates	94	(38)	56
Value at December 31, 2022	**2,602**	**(2,362)**	**240**

The gross value of property, plant and equipment held under 20 years leases at December 31, 2022 was €519,000 (€1,596,000 in 2021) for a net value of €184,000 (€986,000 in 2021). Allowances for depreciation recorded in 2022 amounted to €328,000 (€426,000 in 2021).

Depreciation and amortization of property, plant and equipment are broken down in the statement of profit or loss as follows:

	For the year ended December 31	
	In €000	
	2022	2021
Research and development expenditures	(22)	(26)
Commercial and administrative expenses	(311)	(407)
Total allowances for depreciation and amortization	**(333)**	**(433)**

9. INTANGIBLE ASSETS

9.1 Breakdown by nature

	At December 31	
	2022	2021
	In €000	
Patent, rights, licenses	78,600	74,136
Software	357	357
Research and development activities acquired separately	50	50
Gross value	**79,007**	**74,543**
Patent, rights, licenses	(46,913)	(34,268)
Software	(352)	(251)
Research and development activities acquired separately	(50)	(50)
Accumulated depreciation	**(47,315)**	**(34,569)**
Net value of intangible assets	**31,692**	**39,974**

At December 31, 2022, the gross value of intangible assets relating to intellectual property amounted to €78.6 million, breaking down as follows:

- €45.7 million, equivalent to US$48.7 million for ZERVIATE (of which €17.4 million, equivalent to US$18.6 million, corresponding to the value allocated to the U.S. territory); the net book value of ZERVIATE allocated to the U.S. territory was fully amortized as of December 31, 2021. The net book value of ZERVIATE after impairment amounted to €28.2 million equivalent to US$30.1 million as of December 31, 2022 and corresponds mainly to the valuation of ZERVIATE for the Chinese and Southeast Asian markets.
- NCX 4251 for €31.0 million equivalent to US$33 million. NCX 4251 was depreciated in the amount of US$17.8 million as of December 31, 2021. An additional impairment charge of US$11.5 million was recorded in 2022 (see Note 4.6). At December 31, 2022, the net value of NCX 4251 after impairment amounted to US$3.7 million (equivalent to €3.5 million) and corresponds exclusively to the territory of China and Southeast Asia. The residual value of the intellectual property associated with NCX 4251 is considered as in process research and development (IP R&D) and as such is not amortized. When the development activities of this product are completed, it will be amortized according to its estimated useful life that will be initially determined on the basis of the patent's remaining life.
- The balance relates to patents having a gross value of €2.0 million having been fully amortized.
- The net book value of IP R&D amounted to €31.7 million at December 31, 2021.

The Group conducted an impairment test for two IP R&D assets in the statement of financial position as previously described (ZERVIATE and NCX 4251). These tests are sensitive to assumptions specific to the nature of the asset. In addition to the discount rate, the main assumptions used in 2022 relate to:

- Medium and long-term forecasts notably concerning the size and penetration rate of the market, and
- The probability of the success for IP R&D projects.

The assumptions used for impairment tests on intangible assets are reviewed at least once a year.

The discount rates after taxes used in 2022 range between 7% and 16%.

9.2 Change in the year

	Gross value	Amortization and depreciation	Net value
		In €000	
Value at December 31, 2020	**68,988**	**(4,140)**	**64,848**
Acquisitions/Amortization	-	(28,980)	(28,980)
Disposals or retirements	-	-	-
Impact of change in exchange rates	5,555	(1,449)	4,106
Reversals	-	-	-
Value at December 31, 2021	**74,543**	**(34,569)**	**39,974**
Acquisitions/Amortization (1)	-	(10,883)	(10,883)
Disposals or retirements	-	-	-
Impact of change in exchange rates	4,464	(1,863)	2,601
Reversals	-	-	-
Value at December 31, 2022	**79,007**	**(47,315)**	**31,692**

(1) Amortization of ZERVIATE and NCX4251 (see Note 4.6)

Amortization and depreciation of intangible assets are broken down in the statement of profit or loss as follows:

	For the year ended December 31	
	2022	2021
	In €000	
Research and development expenditures	-	(1)
Commercial and administrative expenses	(13)	(14)
Amortization of intangible assets	-	(1,205)
Impairment of intangible assets(1)	(10,870)	(27,760)
Total allowances for amortization and depreciation	**(10,883)**	**(28,980)**

(1) Amortization of ZERVIATE and NCX 4251 (see Note 4.6)

10. GOODWILL

Goodwill at December 31, 2022 represents exclusively goodwill of the Group.

	Gross value	Amortization and depreciation	Net value
		In €000	
Value at December 31, 2020	**23,663**	**-**	**23,663**
Impact of change in exchange rates	1,974	-	1,974
Value at December 31, 2021	**25,637**	**-**	**25,637**
Impact of change in exchange rates	1,586	-	1,586
Value at December 31, 2022	**27,223**	**-**	**27,223**

10.1. Goodwill impairment tests

The net book value of goodwill and intangible assets breaks down as follows

	At December 31, 2022		
	Basis for impairment	Amortization and depreciation	Net value
		In €000	
Goodwill	27,223	-	27,223
Intangible assets	79,007	(47,315)	31,692
Total	**106,230**	**(47,315)**	**58,915**

A comparison between value in use and the book value on the statement of financial position was made and subject to sensitivity analysis based on the parameters which included:

- the change in the discount rate;
- the change in the percentage of success of IP R&D projects;
- the change in revenue expected from the Group's different projects.

No impairment of goodwill tested should be recognized in the case of a reasonably possible change in the assumptions used in 2022. On this basis, the following changes will not result in recognition by the Group of a goodwill impairment in the statement of financial position:

- an increase in the discount rate of 10 points above the discount rate currently used;
- a decrease in the percentage of success for projects under development of 20 points below the rate currently used, or;
- a decrease in sales expected from different Group projects of 20 points below the rates currently used;

No impairment of goodwill was recognized in 2022 and 2021.

11. GOVERNMENT GRANTS RECEIVABLE

	At January 1, 2022	Recognized in the period	Reimbursed in the period	At December 31, 2022
Research tax credit	1,452	504	(1,452)	504
Total	**1,452**	**504**	**(1,452)**	**504**

	At January 1, 2021	Recognized in the period	Reimbursed in the period	At December 31, 2021
Research tax credit	737	715	-	1,452
Total	**737**	**715**	**-**	**1,452**

Government subsidies granted to the Group for research and development expenditures incurred under research programs are recognized in *Government grant receivables* for the period during which the expenses related to the grant were incurred, provided that there is reasonable certainty that the Group has met the terms and conditions associated with the grant and that the grant will be received.

12. OTHER CURRENT ASSETS AND PREPAID EXPENSES

Other current assets consist mainly of the following items:

	At December 31	
	2022	2021
	In €000	
Tax receivables [(1)]	1,048	217
Employee-related receivables	32	20
Other receivables	199	140
Total	**1,279**	**377**

(1) Corresponds mainly to a deposit with the French tax authorities of the amount indicated in the tax notice (€774,226) following the tax audit for the years 2016 to 2018 and for which the Company is contesting certain points. The Company is pursuing its appeal process. This amount will be returned to the Company at the end of this procedure if this appeal is successful.

13. OTHER NON-CURRENT FINANCIAL ASSETS

	At December 31	
	2022	2021
	In €000	
Deposits and guarantees	66	237
Sublease receivable [1]	259	-
Total non-current financial assets	**325**	**237**

(1) Receivable relating to the sublease of the offices of the American subsidiary whose lease expires in June 2025. The branch is now using a coworking facility.

14. CASH AND CASH EQUIVALENTS

	At December 31	
	2022	2021
	In €000	
Cash	11,052	31,970
Cash equivalents [1]	16,598	10,000
Total cash and cash equivalents	**27,650**	**41,970**

(1) Cash equivalents consist of time deposit accounts. In accordance with the IAS 7 criteria, these are considered to meet the definition of cash equivalents.

15. ISSUED CAPITAL AND RESERVES

At December 31, 2022, the share capital of the Group consists of 50,100,448 fully paid up ordinary shares with a par value of €1.

	Share capital	Share premium	Number of shares	Par value
	In €000			
At December 31, 2020	**37,031**	**528,595**	**37,030,335**	**1**
Issuance of ordinary shares*	6,000	7,712	6,000,000	
Share-based payments	107	(107)	107,850	
At December 31, 2021	**43,138**	**536,200**	**43,138,185**	**1**
Issuance of ordinary shares**	6,849	2,115	6,849,316	
Share-based payments	113	(113)	112,947	
At December 31, 2022	**50,100**	**538,202**	**50,100,448**	**1**

* Capital increase without preferential subscription rights reserved for companies or French or foreign investment funds investing in the pharmaceutical/biotechnology sector. This capital increase resulted in the issue of 6,000,000 new ordinary shares, each share with an attached warrant to acquire 5,100,000 additional new ordinary shares, Gross proceeds from this issue amounted to €15 million.

** Capital increase without preferential subscription rights reserved for companies or French or foreign investment funds investing in the pharmaceutical/biotechnology sector. This capital increase resulted in the issue of 6,849,316 new ordinary shares, each share with an attached warrant to acquire 6,849,316 additional new ordinary shares for a total gross amount of €10 million (see Note 4.7).

Options with a potentially dilutive effect

15.1 Stock options

The Group has a stock option plan for its employees and corporate officers (See Note 16.1).

Changes in the period are described below:

	Rights	Number of shares issuable
Options outstanding at December 31, 2021*	**904,250**	**904,250**
Awarded in the period	2,541,800	2,541,800
Canceled or expired in the period	- 405,150	- 405,150
Exercised in the period	-	-
Options outstanding at December 31, 2022	**3,040,900**	**3,040,900**

*137,300 stock options granted in 2020 and 2021 were canceled retroactively by the Board of Directors on April 7, 2022

15.2 Warrants

The Board of Directors issued stock warrants to certain directors and members of the Glaucoma Clinical Advisory Board authorized by the General Meeting (See Note 16.2).

Changes in the period are described below:

Number of warrants issuable	
Equity warrants outstanding at January 1, 2022	**348,000**
Awarded in the period	-
Canceled or lapsing in the period	-144,000
Equity warrants outstanding at December 31, 2022	**204,000**

15.3 Restricted stock units (*actions gratuites* or free shares)

As from the first half of 2007, the Group introduced a plan for granting restricted stock units to various Group employees (See Note 16.3).

Changes in the period are described below:

	Rights	Number of shares issuable
Restricted stock units outstanding at December 31, 2021	**254,400**	**254,400**
Awarded in the period	959,700	959,700
Canceled or expired in the period	154,903	154,903
Delivered in the period	112,947	112,947
Restricted stock units outstanding at December 31, 2022	**946,250**	**946,250**

16. SHARE-BASED PAYMENTS

The Board of Directors sets the Group's objectives each year. Achieving these objectives is one of the criteria upon which variable compensation is calculated for certain employees. Furthermore, Group employees and Directors receive share-based compensation (stock options, restricted stock units and stock warrants). The vesting of this share-based compensation is subject to performance conditions requiring that at least 50% of the Group's yearly objectives set by the Board of Directors are met for the calendar year concerned. In the event that these performance conditions are not met, half of the rights granted for 2022 (i.e. 50% + 1 right) will be definitively canceled, with the other half of the rights remaining in effect for the stock options and restricted stock units.

16.1 Stock subscription or purchase options

On October 22, 2014, the general meeting approved a stock option plan for employees and corporate officers and authorized the Board of Directors to grant options entitling the holder to subscribe for a maximum of 200,000 outstanding or new ordinary shares (understood as after the reverse stock split on December 3, 2015) with a par value of €1. The vesting of these options is subject to performance conditions set by the Board of Directors at the time of the grant. The Board of Directors determines the identity of the grantees as well as the conditions and criteria for granting the options. The options granted under this authorization must be exercised no later than six years after the effective award date by the Board of Directors. This authorization, granted for a period of 38 months from the date of the meeting, was rendered void by the general meeting of June 3, 2015, but no option was granted under this authorization of this General Meeting.

On May 24, 2018, the General Meeting granted an authorization to the Board of Directors for 38 months to award 1,000,000 stock options or stock purchase options to Group employees and officers. The exercise of these options is subject to performance conditions for beneficiaries who are members of the Executive Committee, set by the Board of Directors at the time of the grant. The options granted under this authorization must be exercised no later than eight years after the effective award date by the Board of Directors. This authorization, granted for a period of 38 months from the date of the meeting, was rendered void by the general meeting of June 30, 2020.

On June 30, 2020, the General Meeting granted an authorization to the Board of Directors for 38 months to award 1,000,000 stock options or stock purchase options to Group employees and officers. The exercise of these options is subject to performance conditions for beneficiaries who are members of the Executive Committee, set by the Board of Directors at the time of the grant. The options granted under this authorization must be exercised no later than eight years after the effective award date by the Board of Directors.

On April 28, 2021, the General Meeting granted an authorization to the Board of Directors for 38 months to award 2,500,000 stock options or stock purchase options to Group employees and officers. The exercise of these options is subject to performance conditions for beneficiaries who are members of the Executive Committee, set by the Board of Directors at the time of the grant. The options granted under this authorization must be exercised no later than eight years after the effective award date by the Board of Directors.

On July 28, 2022, the General Meeting granted an authorization to the Board of Directors for 38 months to award 2,500,000 stock options or stock purchase options to Group employees and officers. The exercise of these options is subject to performance conditions for beneficiaries who are members of the Executive Committee, set by the Board of Directors at the time of the grant. The options granted under this authorization must be exercised no later than eight years after the effective award date by the Board of Directors.

Stock options granted between January 1, 2015 and December 31, 2021 were subject to achieving 70% of the conditions of performance which have been consistently met. From January 2022 onwards, the percentage of the conditions of performance to be achieved was changed to 50%.

The following table presents, at December 31, 2022, the outstanding options issued under these plans:

Board of Directors' meeting date	Options granted	Exercise date of the options	Expiry date	Subscription price per option in euros	Number of canceled or expired options	Options outstanding	Number of outstanding shares issuable upon exercise of the options
Plan authorized by the General Meeting of 10/22/2014							
01/30/2015	200,000	01/30/2019	01/30/2021	€1.8700	200,000	0	0
	200,000				**200,000**	**0**	**0**
Plan authorized by the General Meeting of 05/24/2018							
02/12/2019	176,550	02/12/2021	02/12/2027	€6.0546	54,150	122,400	122,400
01/27/2020	394,750	01/27/2022	01/27/2028	€4.7910	84,600	310,150	310,150
	571,300				**138,750**	**432,550**	**432,550**
Plan authorized by the General Meeting of 06/30/2020							
10/15/2020	56,000	10/31/2021	10/15/2028	€2.9200	40,000	16,000	16,000
10/15/2020	56,000	10/31/2022	10/15/2028	€2.9200	40,000	16,000	16,000
01/14/2021	349,550	01/14/2023	01/14/2029	€3.5181	56,000	293,550	293,550
	461,550				**136, 000**	**325,550**	**325,550**
Plan authorized by the General Meeting of 04/28/2021							
02/15/2022	457,500	02/15/2024	02/15/2030	€2.3716	47,700	409,800	409,800
04/07/2022	52,000	04/08/2022	04/07/2030	€2.9200	36,000	16,000	16,000
04/07/2022	52,000	10/31/2022	04/07/2030	€2.9200	36,000	16,000	16,000
04/07/2022	33,300	01/14/2023	04/07/2030	€3.5181	24,300	9,000	9,000
07/01/2022	286,666	06/01/2023	07/01/2030	€1.7954	0	286,666	286,666
07/01/2022	286,666	06/01/2024	07/01/2030	€1.7954	0	286,666	286,666
07/01/2022	286,668	06/01/2025	07/01/2030	€1.7954	0	286,668	286,668
07/19/2022	328,673	07/19/2023	07/18/2030	€1.7965	36,668	292,005	292,005
07/19/2022	328,664	07/19/2024	07/18/2030	€1.7965	36,666	291,998	291,998
07/19/2022	15,000	07/19/2024	07/18/2030	€1.7965	5,000	10,000	10,000
07/19/2022	328,663	07/19/2025	07/18/2030	€1.7965	36,666	291,997	291,997
	2,455,800				**259,000**	**2,196,800**	**2,196,800**
Plan authorized by the General Meeting of 07/28/2022							
09/23/2022	28,670	09/23/2023	09/23/2030	€1.9000	0	28,670	28,670
09/23/2022	28,665	09/23/2024	09/23/2030	€1.9247	0	28,665	28,665
09/23/2022	28,665	09/23/2025	09/23/2030	€1.9247	0	28,665	28,665
	86,000				**0**	**86,000**	**86,000**
	3,774,650				**733,750**	**3,040,900**	**3,040,900**

The following table illustrates the number and weighted average exercise prices of the options proposed in the plan:

	Number of options	Number of shares	Weighted average exercise price of the shares corresponding to the options (in euros)
Options outstanding at start of period	**904,250**	**904,250**	**€4.33**
Granted during the period	2,541,800	2,541,800	€1.97
Canceled	(405,150)	(405,150)	€2.91
Outstanding at end of period	**3,040,900**	**3,040,900**	**€2.55**

The weighted average remaining contractual life of the outstanding stock options is 7 years and 2 months as of December 31, 2022 (6 years and 6 months as of December 31, 2021).

In accordance with IFRS 2, the stock options were remeasured. The impact of the stock option valuation on Group income represented an expense of €687,000 at December 31, 2022 (2021: €886,000)

16.2 Warrants

On May 30, 2017, the General Meeting approved the principle of a capital increase of €144,000 by issuing without consideration 144,000 equity warrants conferring rights to the holder to a maximum of 144,000 new shares at a par value of €1 per share for six members of the Board of Directors. These warrants were issued by the Board of Directors on June 8, 2017 and must be exercised within five years from their issue date. These warrants were subject to conditions of performance set by the Board when the rights were granted and which were noted by the Board in December 2017 as having been fulfilled.

On May 24, 2018, the General Meeting approved in principle a capital increase of €300,000 by issuing without consideration 300,000 equity warrants entitling the holders to a maximum of 300,000 new shares at a par value of €1 per share in favor of the Board of Directors' six members at that time (Ms. Birgit Stattin Norinder having resigned effective June 20, 2018). 144,000 warrants were issued by the Board of Directors on May 25, 2018 and must be exercised within five years from their issue date. These warrants were subject to conditions of performance set by the Board when granted, and which were noted by the Board in September 2018 as having been fulfilled.

On June 30, 2020, the General Meeting of the shareholders approved in principle a capital increase of €60,000 through the issue, free of charge, of 60,000 equity warrants conferring rights to a maximum of 60,000 new ordinary shares at a par value of € 1 for six members of the Company's glaucoma clinical advisory board. These warrants were subject to conditions of performance set by the Board when granted, and which in September 2020 the Board recognized as having been fulfilled.

The following table presents, at December 31, 2022, the equity warrants outstanding:

	Plan 7	*Plan 8*	*Plan 9*
Shareholders' meeting date	May 2017	May 2018	June 2020
Board of Directors' meeting date	June 08, 2017	May 25, 2018	July 16, 2020

Total number of shares that may be subscribed	144,000	144,000	60,000
Expiration date	June 07, 2022	May 24, 2023	July 15, 2025
Warrant exercise price (€)	11.8841	8.8803	4.1449
Exercise methods	(1)	(1)	
Number of shares subscribed at December 31, 2022	-	-	-
Aggregate number of equity warrants canceled or expired	144,000	-	-
Equity warrants remaining at end of year	0	144,000	60,000

(1) The exercise of the warrants was contingent on the Company's Board of Directors' determination that the Company completed certain undisclosed strategic objectives, which was the case.

The valuation of the warrants had no impact on Group results in 2022 and 2021. The following table illustrates the number and weighted average exercise prices proposed in the plan:

	At December 31, 2022		
	Number of options	**Number of shares**	**Weighted average exercise price of the shares corresponding to the options (in euros)**
Outstanding at start of the period	**348,000**	**348,000**	**9.31**
Granted during the period	-	-	-
Canceled or lapsed during the period	- 144,000	- 144,000	11.88
Outstanding at end of period	204,000	204,000	7.49
Exercisable at end of period	**204,000**	**204,000**	**7.49**

16.3 Restricted stock units (*actions gratuites* or free shares)

On May 24, 2018, the General Meeting authorized the Board of Directors to award the Group's employees and corporate officers, without consideration, for a period of 38 months, a maximum of 1,000,000 outstanding or new ordinary shares of the group with a par value of €1 each. The vesting of these shares is subject to performance conditions set by the Board of Directors at the time of the grant.

The vesting of restricted stock units granted in 2018 under the May 24, 2018 plan was contingent, for certain rights, on the Board of Directors' determination of the achievement of at least 70% of the annual objectives of the Group. In January 2019, the Board of Directors duly noted that 90% of the Group's undisclosed objectives were met.

The vesting of restricted stock units granted in 2019 under the May 24, 2018 plan was contingent, for certain rights, on the Board of Directors' determination of the achievement of at least 70% of the annual

objectives of the Group. In March 2020, the Board of Directors duly noted that 90% of the Group's undisclosed objectives were met.

The vesting of restricted stock units granted in 2020 under the May 30, 2017 plan was contingent on the Board of Directors' determination of the achievement of at least 70% of the annual objectives of the Group. In December 2020, the Board of Directors duly noted that 100% of the Group's undisclosed objectives were met.

On April 28, 2021, the General Meeting authorized the Board of Directors to award the Group's employees and corporate officers, without consideration, for a period of 38 months, a maximum of 1,000,000 outstanding or new ordinary shares of the group with a par value of €1 each. The vesting of these shares is subject to performance conditions set by the Board of Directors at the time of the grant.

The vesting of restricted stock units granted in 2021 under the April 02, 2021 plan was contingent, for certain rights, on the Board of Directors' determination of the achievement of at least 70% of the annual objectives of the Group. In December 2021, the Board of Directors duly noted that 70% of the Group's undisclosed objectives were met.

The vesting of restricted stock units granted in 2022 under the May 05, 2021 plan was contingent, for certain rights, on the Board of Directors' determination of the achievement of at least 50% of the annual objectives of the Group. In January 2023, the Board of Directors duly noted that 100% of the Group's undisclosed objectives were met.

On July 28, 2022, the General Meeting authorized the Board of Directors to award the Group's employees and corporate officers, without consideration, for a period of 38 months, a maximum of 1,000,000 outstanding or new ordinary shares of the group with a par value of €1 each. The vesting of these shares is subject to performance conditions set by the Board of Directors at the time of the grant.

The vesting of the restricted stock units granted in 2022 under the plan authorized on September 14, 2022 was contingent on the Board of Directors recognizing the activation of three additional sites in the United States before December 31, 2022 as part of the ongoing Denali clinical study. In January 2023, the Board of Directors duly noted that 100% of the Group's undisclosed objectives were met.

The following table presents, at December 31, 2022, the restricted stock units issued under these plans:

Board of Directors' meeting date	Shares granted	Vesting date of shares	Number of ordinary canceled	Vested shares	Total issuable
Plan authorized by the General Meeting of 05/24/2018					
02/12/2019	83,650	02/12/2021	10,000	73,650	0
04/19/2019	8,000	04/19/2021	0	8,000	0
05/24/2019	1,400	05/24/2021	0	1,400	0
07/11/2019	12,000	07/11/2021	0	12,000	0
09/16/2019	12,800	09/16/2021	0	12,800	0
01/27/2020	99,750	01/27/2022	14,800	84,950	0
03/05/2020	8,000	03/05/2022	8,000	0	0
08/05/2020	24,000	08/05/2022	12,000	12,000	0
10/15/2020	54,000	10/15/2022	38,003	15,997	0
	303,600		**82,803**	**220,797**	**0**
Plan authorized by the General Meeting of 06/30/2020					
01/14/2021	83,150	01/14/2023	26,900	0	56,250
	83,150		**26,900**	**0**	**56,250**
Plan authorized by the General Meeting of 04/28/2021					
05/05/2021	13,800	05/05/2023	0	0	13,800
07/19/2021	2,400	07/19/2023	2,400	0	0
12/16/2021	9,000	12/16/2023	9,000	0	0
01/12/2022	33,700	01/12/2024	11,500	0	22,200
02/15/2022	129,600	02/15/2024	16,000	0	113,600
07/19/2022	725,400	07/19/2024	56,000	0	669,400
	913,900		**94,900**	**0**	**819,000**
Plan authorized by the General Meeting of 07/28/2022					
09/23/2022	71,000	09/23/2024	0	0	71,000
	71,000		**0**	**0**	**71,000**
	1,371,650		204,603	220,797	946,250

The impact of the valuation of restricted stock units on Group income represented €496,000 at December 31, 2022 (2021: €577,000).

17. CURRENT AND NON-CURRENT PROVISIONS

	At Jan. 1, 2022	Increase	Actuarial gains and losses	Amount used in the period	Change in consolidation scope	At Dec. 31, 2022
			In €000			
Post-employment obligations*	661	51	(134)	-	-	578
Total provisions	**661**	**51**	**(134)**	**-**	**-**	**578**
Non-current provisions	*661*	51	*(134)*	-	-	578
Current provisions	-	-	-	-	-	-

* See Note 18.1

18. POST-EMPLOYMENT OBLIGATIONS

The Group has an unfunded defined benefit pension plan that covers all employees of Nicox S.A. This plan is governed by the provisions of the Company's collective agreement and entitles all employees with at least five years of service to receive, upon retirement, payment equal to three-tenths of a month's salary per year from the date of hire up to a maximum of nine months' salary.

The main actuarial assumptions used to measure the defined-benefit obligation are as follows:

	At December 31	
	2022	2021
Social security contribution rate	45.20%	45.20%
Salary increases	2.50%	2.0%
Discount rate [(1)]	3.70%	0.88%
Conditions of retirement	voluntary	voluntary
Retirement age:	Management: 65 years Non-management: 63 years	Management: 65 years Non-management: 63 years

(1) The rate adopted for the purpose of this evaluation corresponds to the average between the IBOXX Corporates AA rate and the 15-year Bloomberg Rate.

The table below presents the reconciliation between the opening and closing balances of net defined benefit obligations and their components:

	In €000
At Jan. 1, 2021	**730**
Costs of services rendered during the period	(69)
Finance expenses	2
Actuarial gains and losses	(2)
At Dec. 31, 2021	**661**
Costs of services rendered during the period	45
Finance expenses	6
Actuarial gains and losses	(134)
At Dec. 31, 2022	**578**

19. DEFERRED INCOME

Deferred income amounted to € 2,183,733 at December 31, 2022 (2021: €1,970,000) and corresponds mainly to deferred income recognized in connection with the amendment to the license agreement with Ocumension for NCX 470 (see Note 4.2). This revenue will be recognized only if it becomes highly probable that the uncertainty associated with the variable consideration is subsequently resolved and the potential repayment clauses do not result in an adjustment involving a significant decrease in the cumulative amount of revenue recognized.

20. CURRENT AND NON-CURRENT FINANCIAL LIABILITIES

	At December 31	
	2022	2021
	In €000	
Borrowings [(1)]	20,039	20,520
Put liability (2)	4,181	
Leases	386	640
Total non-current financial liabilities	**24,606**	**21,160**

	At December 31	
	2022	2021
	In €000	
Borrowings [(1)]	496	-
Leases	332	346
Total current financial liabilities	**828**	**346**

(1) See Note 4.3.

(2) See Note 4.7.

Financial liabilities under the "Borrowings" line item of the above table are comprised exclusively of fixed rate debt. With the exception of the lease liabilities of the US entity denominated in US dollars, all other financial liabilities are in euros. (see 4.3)

In €000	Nominal	Maturity	Fair value (debt component) at the restructuring date	Net book value as at 12/31/2022	EIR
Non-convertible bond [(1)]	11,870	1 Jul. 2026	11,733	11,744	9.4%
Convertible bond	3,300	January 1, *2026*	*3,268*	3,276	9.5%
Non-convertible bond with repayment premium	1,787	January 1, 2026	3,503	3,680	9.2%
	16,957		**18 504**	**18,700**	

[(1)]Extension by 6 months (i.e. to July 1, 2026) due to a favorable response to the primary efficacy endpoint of non-inferiority to latanoprost in the Mont-Blanc clinical trial.

21. DEFERRED TAX LIABILITIES

At December 31, 2022, deferred tax liabilities amounted to €7,340,000 (2021: €9,237,000). This corresponds to deferred tax liabilities calculated on the basis of fair value adjustments associated with the exercise of the purchase price allocation of the US subsidiary, Nicox Ophthalmics Inc., net of deferred tax assets. The change in 2022 reflects the reversal of the deferred tax liability of €2,498,000 (US$2,633,000) arising from the amortization of NCX4251 and the foreign exchange translation adjustment of €601,000. The Group has tax losses in France and in the United States. In 2019, the Group conducted a study of tax losses available for use by the US subsidiary. In compliance with article 382 of the US Internal Revenue Code (IRC) concerning historical losses available to be carried forward, the Group considered that it does have tax loss carryforwards with respect to federal and state taxes incurred prior to the Nicox Opthalmics, Inc.'s acquisition for an amount of US$50.9 million eligible to be carried forward to offset taxable income for the statutory period of 20 years. In addition, tax losses generated in the United States since the US tax reform adopted by the U.S. Senate on December 2, 2017 and tax loss carryforwards generated in France do not expire. Tax loss carryforwards generated in France may be applied to tax profit for up to 50% of their amount in a given year. With the exception of deferred tax assets recognized to offset deferred tax liabilities on equity warrants relating to the loan agreement in France and deferred tax assets relating to development activities completed in 2019 in the United States recognized to offset the corresponding deferred tax liabilities, no deferred tax asset was recognized in the consolidated statements of the financial position at December 31, 2022 and December 31, 2021, as the Group was unable to assure that it would be able to recover the tax credit on possible taxable income in the foreseeable future.

Loss carryforwards:	**At December 31**	
	2022	**2021**
	In €000	

Parent company (1)	490,218	497,366
US subsidiary (2)	77,421	69,150
Total Group loss carryforwards	**567,639**	**566,516**

(1) Net of €24.8 million in tax loss carryforwards abandoned pursuant to a challenge by the tax authorities (see Note 6)
(2) The U.S. subsidiary also benefits from €3.3 million (or US$3.6 million) in research tax credits that will begin to expire in 2027 if not used.

22. OTHER CURRENT LIABILITIES

	At December 31	
	2022	2021
	In €000	
VAT payables	218	172
Provisions relating to personnel expenses	1,666	1,613
Other	209	250
Total other current liabilities	**2,093**	**2,035**

23. OFF-BALANCE SHEET COMMITMENTS

The Group has a number of commitments from its partners for potential royalty payments contingent on the materialization of future events. The most significant agreements are described below:

23.1 Licensing agreements

- **Bausch + Lomb**

In March 2010, the Group signed a licensing agreement with Bausch & Lomb (a Valeant company), a leading eye health company, granting Bausch & Lomb exclusive worldwide rights to develop and market VYZULTA (latanoprostene bunod ophthalmic solution, 0.024%). Under the terms of the agreement, Bausch + Lomb made an initial license payment of $10 million to the Group upon execution of the agreement. This was followed by an additional €10 million milestone payment in April 2012 pursuant to the decision to pursue development of LATANOPROSTENE BUNOD after the Phase 2b study completion in late 2011. Finally, in 2017 the Group received a US$17.5 million milestone payment following the FDA approval for VYZULTA on November 2, 2017.

The Group stands to receive in the future additional potential payment which could total US$165 million, if certain regulatory and sales milestones are met and which would result in net milestone payments for the Group of up to US$150 million less payments due to Pfizer as part of the 2009 agreement. The Group would also receive potential net royalties on sales ranging from 6% to 12% following payments due to Pfizer.

This agreement will remain in effect until all royalty payment obligations from Bausch + Lomb expire or unless terminated earlier by either the Group or by Bausch & Lomb pursuant to the early termination provision provided for in the agreement. The Group may terminate this agreement on a country-by-country basis if Bausch + Lomb fails to use commercially reasonable efforts to develop and commercialize the

licensed products under this agreement. It may also terminate this agreement in its entirety in the event that Bausch + Lomb challenges or causes a third party to challenge the validity or ownership of any of Nicox's licensed patents or fails or becomes unable to meet its payment obligations under the agreement. In the event of termination, licenses granted by the Group to Bausch + Lomb will be terminated, and any sublicenses granted by Bausch + Lomb will either be assigned to the Group or terminated.

- **Pfizer**

In August 2009, the Group entered into a contract with Pfizer ending their previous collaboration agreements dated August 2004 and March 2006. Under the terms of this contract, the Group recovered all the development and marketing rights for latanoprostene bunod (henceforth under the trade name of VYZULTA), and in particular the right to sub-license, in addition to all the data and development information. This drug is currently out-licensed to Bausch + Lomb (see above) and commercialized since December 2017. Furthermore, the Group has access to certain information regarding the development of Xalatan® (latanoprost) belonging to Pfizer, most notably the regulatory files for Xalatan®. In exchange, the Group has undertaken to pay Pfizer two milestone payments of US$15 million each. The first milestone payment linked to the VYZULTA approval in the United States was paid in December 2017. The second milestone payment is linked to reaching pre-defined sales levels. The Group is also subject the payment of royalties on future sales. The Group also recovered the rights to a number of new nitric oxide-donor compounds at the research stage for the treatment of diabetic retinopathy and glaucoma.

- **Fera Pharmaceutical**

In November 2015, the Group entered into an exclusive license agreement with Fera Pharmaceuticals, a private specialized pharmaceutical company, to develop and commercialize Nicox's naproxcinod in the United States. This agreement provides that Fera will initially focus on the signs and symptoms of osteoarthritis. Fera afterwards plans to seek advice from the United States Food and Drug Administration (FDA) regarding the additional clinical work required before submitting a New Drug Application (NDA) for naproxcinod. Fera Pharmaceuticals will be responsible for, and will fully finance, all clinical development manufacturing and commercialization activities.

Under the terms of the agreement, the Group may be eligible to receive up to $40 million in sales-based milestones, plus 7% royalties based on net sales of naproxcinod in the U.S.

It should be noted that Fera Pharmaceuticals could receive royalties of an undisclosed amount in the event that naproxcinod is approved and commercialized using data generated by Fera Pharmaceuticals, regardless of the therapeutic indication and territory (outside the US). During the second quarter of 2020, Nicox was informed by its partner Fera that the Orphan Drug Designation (ODD) application for naproxcinod in sickle cell disease at the US FDA was denied and that it is currently considering possible responses to the FDA's letter. Fera is also considering alternative indications for the development of naproxcinod including as a potential adjuvant treatment for patients with COVID-19 infection. Nicox and Fera have amended their existing agreement to include COVID-19 as an indication, and Nicox will granted to Fera warrants to acquire 10,000 Nicox shares; In March 2022, Nicox and Fera announced that the United States (U.S.) Food and Drug Administration (FDA) has granted Orphan Drug Designation for naproxcinod for the treatment of sickle cell disease, which affects an estimated 100,000 Americans. Naproxcinod is a nitric oxide (NO)-donating naproxen combining the cyclooxygenase (COX) inhibitory activity of naproxen with that of nitric oxide developed by Nicox and exclusively licensed to Fera in the U.S. Nicox has tested naproxcinod in over 2,700 patients in osteoarthritis, generating a significant package of clinical safety data which is available to support Fera's development of naproxcinod, and ultimately a New Drug Application submission for sickle cell disease.

- **Ocumension Therapeutics**
  - **The agreement concerning NCX470 is described in Note 4.2**
  - **NCX 4251 and ZERVIATE - Agreement for Greater China**

In June 2019, the Group entered into an exclusive license agreement with Ocumension for the development and commercialization of its drug candidate, NCX 4251, for blepharitis in the Chinese market. Ocumension is responsible, at its own cost, for all development activities necessary for the approval of NCX 4251 in the relevant territory, overseen by a Joint Development Committee comprising representatives of both companies. Ocumension was granted exclusive rights for the agreed territory to develop and commercialize NCX 4251 for blepharitis. Under the terms of the agreement, the Group received an upfront payment of US$2.3 million (€2 million) in June 2019. The Group may potentially receive development and sales milestone payments of up US$11.3 million together with tiered royalties of between 5% and 10% on sales of NCX 4251.

In March 2019, the Group entered into an exclusive license agreement for the development and commercialization of Nicox's product ZERVIATE for the treatment of allergic conjunctivitis in the Chinese market. Ocumension received exclusive rights for the agreed territory to develop and commercialize ZERVIATE. The agreement was amended in March 2020, granting Ocumension additional exclusive rights to ZERVIATE in the majority of the Southeast Asian region. Under a new amendment in July 2021, Ocumension paid Nicox US$2 million in full advance payment of the future development and regulatory milestones for ZERVIATE. Nicox remains eligible to receive the same sales milestones of up to US$17.2 million together with tiered royalties of between 5% and 9% of net sales of ZERVIATE by Ocumension. The other terms of the original agreement remain unchanged. Ocumension is responsible, at its own cost, for the conduct of all development activities that will be overseen by a joint governance committee comprising representatives of both companies. In February 2022, Ocumension obtained positive phase 3 clinical trial results for ZERVIATE® in China (see Note 30, subsequent events). ZERVIATE was found to be non-inferior to emedastine difumarate, an antihistamine marketed under the brand name EMADINE®. Subject to any additional data required by the Chinese National Medical Products Administration (NMPA), this Phase 3 trial, in addition to the data package used by the FDA for ZERVIATE in the United States, is expected to be sufficient to support a Chinese New Drug Application.

In September 2017, the Group entered into an exclusive licensing agreement with Eyevance for the commercialization of ZERVIATE in the United States. Under the terms of the agreement, Eyevance made a one-time upfront nonreimbursable payment in 2017 of US$6 million to the Group followed by a US$3 million milestone payment in July 2019 triggered by the completion of the regulatory and manufacturing activities under Nicox's responsibility. The Group remains eligible for up to $37.5 million in milestones payable on Eyevance achieving pre-defined sales targets, with $30 million of these milestones being triggered by annual sales of $100 million and above. In addition, the Group will also receive tiered royalties of 8% to 15% based on future net sales of ZERVIATE. The Group has also undertaken to pay Eyevance US$ 366,966, linked to the manufacturing costs resulting from delays in completing certain activities. This accrued expense is offset by a portion of royalties paid by Eyevance until settlement of the full amount due.

- **Samil Pharmaceutical Co., Ltd**

In December 2019, Nicox signed an exclusive license agreement with Samil Pharmaceutical Co., Ltd for the development and commercialization of ZERVIATE™ (cetirizine ophthalmic solution), 0.24% for the treatment of ocular itching associated with allergic conjunctivitis in South Korea. Nicox thus granted Samil Pharmaceutical exclusive rights to develop and commercialize ZERVIATE in South Korea. Nicox is eligible to receive 10% royalties on net sales on ZERVIATE in South Korea and a milestone payment of 5% of net sales for each calendar year in which net sales exceed approximately US$900,000. Nicox received an insignificant license fee upon the signature of the agreement in 2021, and may receive in addition approval and launch milestone payments which may total approximately US$189,000. Samil Pharmaceutical will be responsible, at its cost, for the development and commercialization of ZERVIATE in South Korea. ZERVIATE is expected to require manufacturing transfer and associated pharmaceutical

development to support approval in South Korea, in addition to the existing approved U.S. NDA package. In February 2022, the agreement was extended to include Vietnam.

- **ITROM Pharmaceutical**

In August 2020, Nicox granted ITROM exclusive rights to develop and commercialize ZERVIATE in Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Oman, Qatar, the Kingdom of Saudi Arabia, the United Arab Emirates and Yemen. Nicox is eligible to receive 15% royalties on net sales of ZERVIATE in certain key countries, and 10% in other countries. Nicox will also receive a non-significant license fee on signature and may receive a future milestone payment upon the product launch of ZERVIATE. ITROM will be responsible, at its own cost, for development and commercialization of ZERVIATE in the countries covered in the agreement. ZERVIATE is expected to require only the existing approved U.S. New Drug Application (NDA) package to support approval.

- **Laboratorios Grin**

In May 2021, Nicox granted Grin rights to develop and commercialize cetirizine ophthalmic solution, 0.24% in Mexico. Upon signature, Nicox received an undisclosed license fee and potential milestone payments linked to regulatory approval and sales and may receive royalties based on a double-digit percentage of net sales of ZERVIATE. Grin will be responsible, at its own cost, for the development, manufacturing and the commercialization of ZERVIATE in Mexico.

23.2. Other financial commitments payable

23.2.1 Kréos commitment

The Company has given off-balance sheet commitments in connection with the Kréos loan, which are described in Note 4.3.

23.2.2 R&D commitment

To the Group's knowledge, the commitments included in the following table represent all the Group's material off-balance sheet commitments in addition to the items described above.

Contractual obligations	Total	Payments due by period		
		Less than one year	One to five years	More than five years
Research and Development commitments (€ 000s)	15,902 [(1)]	8,534	7,368	
Total				

[(1)] €12,675,000 relate to costs that the Group is expected to be required to pay for the Mont Blanc trials; as contractually agreed, 50% of those costs will be recharged to Ocumension (net of chargebacks: €2,854,000 within one year and €3,484,000 between one and five years).

24. OBJECTIVES, POLICIES AND CAPITAL MANAGEMENT PROCEDURES

To date, the financing needs of the Group have primarily been met by (1) raising funds in financial markets through capital increases by issuing new shares, (2) revenues from license agreement with partners, (3) the

reimbursement of research tax credit receivables and (4) a bond financing agreement. The immediate objective of the Group in terms of capital management is to effectively manage its capital resources to ensure the financing of its research and development activities.

25. FINANCIAL RISK MANAGEMENT OBJECTIVES AND POLICIES

The Group's principal investments are short-term deposits.

25.1. Foreign exchange risk

The Group reports financial information in euros. The majority of the Group's expenses is denominated in US dollars. In fiscal 2022, approximately 61.53% of operating expenses were in US dollars (66.4% in 2021).

Royalty payments and milestone payments denominated in US dollars expected by the Group, and in particular through the exclusive worldwide license agreement granted to Bausch + Lomb for VYZULTA, are not of sufficient size for fluctuations in the euro's value against the US dollar to have a material impact on the Group's operating results.

Nicox Group does not have significant receivables subject to foreign exchange risks.

Nicox Group holds US dollar bank accounts that are translated into euros in the consolidated financial statements at the year-end exchange rate and could be impacted by a significant fluctuation in the €/$ exchange rate. This risk is however mitigated by the fact that cash is exclusively intended to cover the Nicox Group's dollar-denominated expenses resulting from its research and development activities carried out in the United States over the medium term. This concerned cash of €7,667,000 as of December 31, 2022, 27.7% of total cash and cash equivalents.

The Group does not use derivative products or specific internal procedures to limit its risk to foreign exchange exposure.

The Group does not hold financial assets or bank debt that are denominated in foreign currency.

25.2. Interest rate risk

The Group is not exposed to the risk of interest rate fluctuations as its cash and cash equivalents consist solely of fixed-rate time deposit accounts. The Group debt is also based on a fixed rate of interest.

25.3. Market risk

At December 31, 2022 the Group did not have any investments in financial instruments and in consequence did not have an exposure to market risk.

25.4. Liquidity risk

At December 31, 2022, the Group did not have any loans with banks that include an early repayment clause.

As part of the restructuring of its bond financing agreement with Kreos Capital (see Note 4.3), €3.3 million of the remaining amount was issued in the form of convertible bonds. The maturity date is January 1, 2026 subject to the same interest rate as the original financing agreement of 9.25% per annum, payable in cash. The convertible loan is secured by the same guarantees already in place for the term loan. This portion of the bond that can be converted into shares at the option of Kreos at any time (after an initial period of 60 days) until maturity on January 1, 2026. The conversion price is €3.67. If the price of Nicox shares does not allow for the conversion of the bonds before the maturity date of July 1, 2026, the total outstanding amount of the Convertible Loan will be due in a single payment at that time.

The Group has a liquidity agreement backed by a market making contract for the share. This exposure is limited to a maximum investment of €1 million. The unrealized loss on this contract at December 31, 2022 amounted to €655,000.

Business activities show a loss and may continue to do so in the short-term. At December 31, 2022, the Group had €27.6 million in cash and cash equivalents (2021: €42 million).

By restructuring its bond financing agreement with Kreos Capital in December 2021, exercising the option in November 2022 to further extend the interest-only period by six additional months, and completing an issue of new shares for €10 million in gross proceeds reserved for specialized institutional investors in November 2022, the Group has extended its cash runway to Q2 2024.

The Group is continuously seeking new sources of financing to ensure the continuity of its research and development activities.

25.5. Credit risk

There is in principle no risk of recovering the receivable linked to the research tax credit, given that it represents a receivable from the French government.

Concerning the Group's other financial assets, and namely cash and cash equivalents, the exposure to credit risk is contingent on the risk of default by the corresponding third parties.

As of December 31, 2022, cash equivalents consisted exclusively of time deposit accounts.

25.6. Fair value

All the Group’s financial assets and liabilities are measured at fair value.

The majority of the Group’s financial liabilities are classified as financial liabilities measured at amortized cost.

26. RELATIONS WITH RELATED PARTIES

Total compensation recognized for directors (6 persons as of December 31, 2022 and 5 persons as of December 31, 2021) and management committee members (5 persons as of December 31, 2022 and December 31, 2021) breaks down as follows:

	At December 31	
	2022	2021
	In €000	
Short-term benefits (1)	(3,206)	(1,570)
Post-employment benefits	(351)	(291)
Other long-term benefits	65	(29)
Share-based payments	(602)	(487)
Total	**(4,094)**	**(2,377)**

(1) Includes €1,020,000 in severance payments to the former Chairman and Chief Executive Officer pursuant to the Board of Directors' decision to terminate his duties effective June 1, 2022.

At December 31, 2022, stock options, restricted stock units and equity warrants outstanding awarded to company directors and members of the Management Committee were distributed as follows:

Type of equity instruments	Exercise price (€)	Number of equity warrants, options or restricted stock units (free shares)	Number of shares issuable	Expiry date
Equity warrants	€8.88	120,000	120,000	05/24/2023
Free shares	-	525,000	525,000	-
Stock options	€6.05	60,000	60,000	02/12/2027
Stock options	€4.79	190,000	190,000	01/27/2028
Stock options	€3.52	180,000	180,000	01/14/2029
Stock options	€2.37	285,000	150,000	02/15/2030
Stock options	€1.80	1,139,998	1,139,998	07/18/2030

27. CONTINGENT LIABILITIES, DISPUTES AND COMMITMENTS TO EMPLOYEES AND CORPORATE OFFICERS

27.1 Litigation

27.1.1 Disputes with Teva Pharmaceutical

Teva Pharmaceutical Industries filed a notice of opposition on November 23, 2016 with the European Patent Office (EPO) against the European patent covering latanoprostene bunod and requested the revocation of the patent as a whole, alleging the absence of novelty or an inventive step. The European patent office rejected this notice of opposition and decided to maintain the patent as delivered. Teva Pharmaceuticals appealed this decision of the EPO on September 12, 2018. On June 20, 2022, Teva withdrew its appeal. On July 7, 2022, the EPO Board of Appeal closed the appeal proceedings. As a result, the EPO's decision is now final and the patent is maintained as granted.

27.1.2 Dispute with Gland Pharma

In connection with its submission of an abbreviated new drug application (ANDA) to the FDA for approval of a generic version of VYZULTA (latanoprostene bunod), Gland Pharma, an Indian company specializing in generic drugs, is claiming, in accordance with standard practice, that the patents covering VYZULTA are invalid. On June 30, 2022, Bausch + Lomb and Nicox filed a joint complaint against Gland Pharma in New Jersey contesting this allegation (with Bausch + Lomb assuming all costs of this proceeding). As a consequence of this lawsuit, the FDA's regulatory review of the ANDA is automatically suspended for a period of 30 months. Under the terms of the license agreement, Bausch + Lomb will pay all costs related to this proceeding while Nicox will assist Bausch + Lomb in providing all necessary documents and information.. This legal proceeding is expected to last for a period of 3 to 4 years. If one or more patents were to be invalidated (within 3 or 4 years), which the Company believes is unlikely, the Company would no longer receive revenue from Bausch + Lomb, it being specified that this would concern revenue generated in the United States.

27.1.3 Dispute with the tax authorities

In February 2019, the Group was informed of a tax audit of the parent company Nicox SA. This audit was completed in September 2020 by a tax deficiency notice concerning €49.6 million in tax loss carryforwards out of a total of €484.6 million available at December 31, 2020 in addition to €0.7 million in withholding tax. The Group strongly contested the merits of these tax adjustments and duly notified the tax authorities by letter on November 10, 2020. In March 2021, the tax authorities withdrew their challenge to a portion of the tax loss carry-forward for €24.8 million. In 2021, after the Group submitted an appeal to a higher authority, the two remaining tax assessments were maintained. In the first half of 2022, a €0.7 million withholding tax was assessed and paid by the Group. The Group filed a claim regarding the assessment of this amount, which was rejected on September 5, 2022. On November 4, 2022, the Company filed an application with the French Administrative Court for relief from the additional withholding tax, including penalties. The Administrative Court acknowledged receipt of this application on November 8, 2022. The Company has not recorded provisions for this dispute. Concerning the second point of the tax adjustment, i.e. the challenge to the tax loss carryforwards arising from the Company's business activities prior to 2016, the Company decided not to bring the matter before the administrative court and instead corrected its tax loss carryforwards of €24.8 million by reducing their amount in its next tax filing, which should bring an end to the dispute concerning this latter point.

27.1.4 Dispute with URSSAF

The Group contests the application of social security contributions imposed on compensation paid in connection with the offices held by two non-employee directors whose tax residence is in the United States. By judgment of January 24, 2020, the Court of Justice of Nice had approved the claims of the Company. URSSAF appealed this judgment, requesting that it be overturned, the social security charge adjustment confirmed and, as a result, that the Company be ordered to pay €95,054 in principal and €2,000 under Article 700 of the French Code of Civil Procedure. The case was struck from the docket due to the failure of URSSAF to perform procedures. After initiating new procedures, the case was reinstated. After this reinstatement, the case was heard on December 1, 2022 and the judgment was reserved until February 2, 2023 (see Note 29 - subsequent events).

27.2 Commitments to members of the management committee and the corporate officer

Members of the management committee are eligible for a contractual severance benefit of between three and eighteen months of salary should their employment contract be terminated as a result of a change in majority control or the Group within two years from the date thereof. The calculation of this severance benefit is based on salary received by the beneficiaries over the 12 months preceding the termination of the employment contract. Should the employment contract be terminated for all beneficiaries on December 31, 2022, the total amount of the severance benefits payable under the provisions described above would amount to €2,159,860.

Should the employment contract be terminated at the initiative of the Group, the management committee members would also receive a contractual severance payment of between six months' and two years' salary based on the salaries received in the twelve months preceding the termination of the employment contract. The provisions described above do not apply in the case of termination for serious or gross misconduct. In addition, payment of the benefit to the CEO is contingent on the achievement of undisclosed objectives. Should the employment contract be terminated for all beneficiaries on December 31, 2022, the total amount of the severance benefits payable under the provisions described above would amount to

€1,799,228. Due to the conditional nature of the commitments described above, the Group had not recorded any provision at December 31, 2022 for the relevant parties.

28. CONSOLIDATED COMPANIES

Consolidated subsidiary	Date of first-time consolidation	Date of deconsolidation	Registered office	Method of consolidation	Ownership interest (%) 12/31/2021	Ownership interest (%) 12/31/2022
Consolidated subsidiaries:						
Nicox SA	1996	-	2405, route des Dolines 06560 Valbonne Sophia Antipolis, France	Parent	-	-
Nicox S.r.l.	1999	-	Via Ariosto 21, Bresso, MI 20091, Italy	Full consolidation	100%	100%
Nicox Ophthalmics Inc.	2014	-	4819 Emperor Blvd. Suite 400, Durham, NC27703	Full consolidation	100%	100%

29. FEES PAID BY THE GROUP

Auditors' fees paid for 2022 and 2021 break down as follows:

	Ernst & Young Audit				Approbans			
	Amount (before tax)		In %		Amount (before tax)		In %	
	2021	2022	2021	2022	2021	2022	2021	2022
Audit								
External audit, certifications, review of individual and consolidated accounts								
Issuer	161,000	**154,000**	69.73%	75.42%	26,000	28,000	57.78%	73.78%
Consolidated subsidiaries	12,000	**12,000**	5.20%	5.88%				
Other work and services directly associated with the engagement of the external auditor								
Issuer	57,900	**38,202**	25.08%	18.71%	19,000	10,000	42.22%	26.32%
Subtotal	230,900	**204,202**	100.00%	100.00%	45,000	38,000	100.00%	100.00%
Other services rendered by the networks								
Tax-related								
Other (specify if> 10% of audit fees)								
Subtotal								
TOTAL	**230,900**	**204,202**	**100.00%**	100.00%	**45,000**	38,000	**100%**	100.00%

30. SUBSEQUENT EVENTS

The General Meeting of February 28, 2023 approved the transfer of the listing of the Company's shares from Compartment C of the Euronext Paris regulated market to the Euronext Growth Paris multilateral trading facility and gave the Board of Directors full powers to carry out this transfer. The transfer to Euronext Growth Paris, which is subject to the approval of the market undertaking Euronext Paris, was approved by the Euronext Listing Board on April 24, 2023. This operation aims to allow the Company to have its securities admitted to trading on a market more commensurate with its size and market capitalization.

On February 2, 2023, the Court of Appeal upheld the lower court's ruling in the dispute between the Group and Urssaf concerning social security contributions on compensation paid to two non-employee directors who are tax residents of the United States.

PART 4 - ANNUAL FINANCIAL STATEMENTS FOR THE YEAR ENDED DECEMBER 31, 2022

ANNEXE DES COMPTES SOCIAUX 2022

Disclaimer : The Annual Financial Statements for year 2022 are available in French only

NICOX S.A.

2405, route des Dolines, Drakkar D,
06560 Valbonne Sophia Antipolis, France
403 942 642 R.C.S. Grasse

The Annual Financial Statements for year 2022 are available in French only

ACTIF	Notes	Brut	Amortissements &provisions	Net exercice 2022 [12mois]	Net exercice 2021 [12mois]
Frais d'établissement	2.1	58 278	58 278		
Frais de développement	2.1	50 000	50 000		
Concessions, Brevets et droits similaires	2.1	2 819 315	2 818 482	833	1 134
Immobilisations incorporelles	**2.1**	**2 927 593**	**2 926 760**	**833**	**1 134**
Autres immobilisations corporelles	2.2	755 282	729 966	25 316	10 401
Immobilisations corporelles	**2.2**	**755 282**	**729 966**	**25 316**	**10 401**
Participations	2.3	55 631 552	51 700 037	3 931 515	15 431 515
Autres immobilisations financières	2.3	994 177		994 177	1 373 526
Immobilisations financières	**2.3**	**56 625 729**	**51 700 037**	**4 925 692**	**16 805 041**
TOTAL DE L'ACTIF IMMOBILISE		**60 308 604**	**55 356 763**	**4 951 841**	**16 816 576**
Créances clients et comptes rattachés	2.4	2 623 378		2 623 378	1 058 855
Autres créances	2.4	37 844 230		37 844 230	32 607 211
Disponibilités	2.5	27 079 935		27 079 935	41 231 739
Charges constatées d'avance	2.6	1 480 416		1 480 416	2 730 742
TOTAL DE L'ACTIF CIRCULANT		**69 027 959**		**69 027 959**	**77 628 547**
Ecarts de conversion actif		36 393		36 393	
Prime de remboursement des obligations	2.7	1 826 571		1 826 571	
TOTAL DE L'ACTIF		**131 199 527**	**55 356 763**	**75 842 764**	**94 445 123**

PASSIF	Notes	Exercice 2022 [12 mois]	Exercice 2021 [12 mois]
Capital social	2.8	50 100 448	43 138 185
Primes d'émission	2.8	529 547 113	527 545 675
Report à nouveau	2.8	(506 069 207)	(455 731 717)
Résultat de l'exercice	2.8	(31 284 980)	(50 337 492)
TOTAL DES CAPITAUX PROPRES	**2.8**	**42 293 374**	**64 614 651**
Provisions pour risques	2.9	38 724	3 030
Provisions pour charges	2.9	577 729	660 703
PROVISIONS POUR RISQUES & CHARGES	2.9	**616 453**	**663 733**
TOTAL AUTRES FONDS PROPRES			
Emprunts et dettes auprès des établissements de crédit	2.10	21 259 826	18 957 822
Emprunts et dettes financières divers	2.10	4 036 657	3 943 511
Dettes fournisseurs & comptes rattachés	2.10	2 537 119	3 190 399
Dettes fiscales & sociales	2.10	1 071 604	1 086 390
Produits constatés d'avance	2.11	2 169 171	1 970 354
TOTAL DES DETTES		**31 074 377**	**29 148 476**
Ecart de conversion Passif	2.12	**1 858 560**	**18 263**
TOTAL DU PASSIF		**75 842 764**	**94 445 123**

COMPTE DE RESULTAT	Notes	Exercice 2022 [12 mois]	Exercice 2021 [12 mois]
Production vendue de services – refacturation diverses	2.15	211 624	215 093
Redevances pour concessions de brevet	2.15	5 241 677	6 504 239
CHIFFRE D'AFFAIRES	**2.15**	**5 453 301**	**6 719 332**
Reprises sur amortissements et provisions, transferts de charges	2.14	96 594	149 963
Autres produits de gestion courantes	2.15	95	335
TOTAL DES PRODUITS D'EXPLOITATION		**5 549 990**	**6 869 630**
Autres achats et charges externes	2.13	(18 103 353)	(14 573 643)
Impôts, taxes et versements assimilés		(184 054)	(100 687)
Salaires et traitements		(3 052 983)	(2 091 591)
Charges sociales		(1 176 890)	(1 044 282)
Dotations aux amortissements sur immobilisations		(12 679)	(31 029)
Dotations aux provisions pour risques & charges		(41 060)	(44 690)
Autres charges	2.16	(2 241 132)	(1 652 304)
CHARGES D'EXPLOITATION		**(24 812 152)**	**(19 538 226)**
RESULTAT D'EXPLOITATION		**(19 262 162)**	**(12 668 596)**
Autres intérêts et produits assimilés	2.17	1 119 815	489 670
Produit sur cessions de valeurs mobilières de placement	2.17	838	73 324
Reprises sur provisions et transferts de charges	2.17	3 030	2 242 524
Différences positives de change	2.17	872 150	1 073 509
PRODUITS FINANCIERS		**1 995 833**	**3 879 027**
Dotations financières aux amortissements et provisions	2.17	(12 142 298)	(40 203 069)
Intérêts et charges assimilées	2.17	(1 582 377)	(1 515 894)
Différences négatives de change	2.17	(401 012)	(90 186)
Charge sur la cession du prêt obligataire et participation minoritaire	2.17	(48 485)	(48 121)
Charges sur cessions de valeurs mobilières de placement	2.17	(348 851)	(406 977)
CHARGES FINANCIERES		**(14 523 023)**	**(42 264 247)**
RESULTAT FINANCIER		**(12 527 190)**	**(38 385 220)**

COMPTE DE RESULTAT (suite)	Notes	Exercice 2022 [12 mois]	Exercice 2021 [12 mois]
RESULTAT COURANT AVANT IMPOTS		**(31 789 352)**	**(51 053 816)**
RESULTAT EXCEPTIONNEL		**-**	**-**
Crédit impôt recherche - (Impôt sur les bénéfices)	2.22	(504 372)	(716 324)
TOTAL DES PRODUITS		7 545 823	10 748 657
TOTAL DES CHARGES		(38 830 803)	(61 086 149)
PERTE		**(31 284 980)**	**(50 337 492)**

1. NATURE DE L'ACTIVITE ET PRINCIPES COMPTABLES

1.1. Nature de l'activité

Nicox S.A (« la Société ») est domiciliée en France. Le siège social de la Société est situé 2405 route des Dolines, Drakkar 2, Bât D, 06560 Valbonne. La Société est cotée sur Euronext Paris (COX.PA), a un centre de recherche et de développement préclinique en Italie et un centre de développement aux États-Unis.

Nicox est une société internationale spécialisée en ophtalmologie développant des solutions innovantes visant au maintien de la vision et à l'amélioration de la santé oculaire. Nicox a un programme en phase 3 de développement clinique dans le glaucome (la première étude a été achevée, la seconde étude est en cours), un candidat médicament à un stade de développement préclinique dans les maladies de la rétine, un candidat médicament au stade de développement dans la sécheresse oculaire avec un partenaire, licencié pour le marché chinois, et deux produits licenciés commercialisés par des partenaires exclusifs.

- NCX 470, un nouveau collyre bimatoprost donneur d'oxyde nitrique (NO) est en phase 3 de développement clinique pour la réduction de la pression intraoculaire (PIO) chez des patients atteints de glaucome à angle ouvert ou d'hypertension oculaire. L'étude Mont Blanc, la première des deux études cliniques de phase 3 a été achevée et les résultats annoncés en octobre 2022. La deuxième étude de phase 3 Denali, est actuellement en cours et les résultats sont attendus en 2025. Les études Mont Blanc et Denali ont été conçues afin de se conformer aux exigences réglementaires pour des études de sécurité et d'efficacité de phase 3 pour des demandes d'autorisation de mise sur le marché aux Etats-Unis et en Chine. Deux études de phase 3b supplémentaires visant à évaluer le mécanisme d'action double du NCX 470 dans la réduction de la PIO et les potentiels effets bénéfiques du NCX 470 sur la rétine devraient démarrer au premier semestre 2023. Nicox recherche des partenariats pour le NCX 470 pour les marchés américain et japonais. Le NCX 470 fait l'objet d'un accord de licence exclusif avec Ocumension Therapeutics pour la Chine et l'Asie du Sud-Est.

- VYZULTA®, indiqué pour la réduction de la PIO chez les patients atteints de glaucome à angle ouvert ou d'hypertension oculaire, fait l'objet d'un accord de concession de licence exclusif mondial avec Bausch + Lomb. VYZULTA est commercialisé dans plus de 15 pays, dont les Etats-Unis, et est également approuvé dans un certain nombre d'autres pays.

Le Conseil d'administration a arrêté les états financiers sociaux du 31 décembre 2022 le 17 mars 2023.

1.2. Principes comptables

Les états financiers ont été établis en conformité avec le règlement de l'Autorité des Normes Comptables N° 2016-07 du 4 novembre 2016, modifiant le règlement No 2014-03 relatif au plan comptable général, qui a été homologué par arrêté du 26 décembre 2016.

Les conventions générales comptables ont été appliquées en conformité avec le Plan Comptable Général, dans le respect du principe de prudence, et suivant les hypothèses de base suivantes :

- Continuité de l'exploitation,
- Indépendance des exercices,
- Permanence des méthodes comptables d'un exercice à l'autre,

et conformément aux règles générales d'établissement et de présentation des comptes annuels.
Seules sont exprimées les informations significatives. Sauf mention contraire les montants sont exprimés en Euros.

La méthode de base retenue pour l'évaluation des éléments inscrits en comptabilité est la méthode des coûts historiques.

Les principales méthodes utilisées sont présentées ci-après.
La Société a préparé ses comptes sociaux conformément au principe de continuité d'exploitation
Les comptes arrêtés au 31 décembre 2022 ne seront définitifs qu'après leur approbation par l'Assemblée générale des actionnaires.

1.2.1 - Immobilisations incorporelles

Les immobilisations incorporelles sont évaluées à leur coût d'acquisition. Leur amortissement est calculé selon la méthode linéaire sur leur durée de vie économique, selon les modalités suivantes :

Frais de recherche et développement

Les frais de recherche sont intégralement comptabilisés en autres achats et charges externes de l'exercice au cours duquel ils ont été encourus. L'intégralité des frais de développement engagés par la Société est comptabilisée en charge, les critères d'activation n'étant remplis à ce jour par aucun des candidats-médicaments développés par la Société. En effet, en raison des risques et incertitudes liés aux autorisations réglementaires et au processus de recherche et de développement, les critères d'immobilisation ne sont pas réputés remplis avant l'obtention de l'autorisation de mise sur le marché des médicaments. Par conséquent, les frais de développement (principalement des coûts de sous-traitance d'études cliniques et de coûts de production de principe actif de candidats-médicaments) ont toujours été comptabilisés en charge sur la ligne « Autres achats et charges externes ». A ce jour, la Société n'a jamais obtenu d'AMM sur l'un de ses produits développés exclusivement en interne.

Le médicament VYZULTA licencié auprès de son partenaire Bausch & Lomb a été approuvé par la FDA américaine en novembre 2017, la Société n'était plus impliquée dans le développement de VYZULTA depuis l'octroi des droits mondiaux à son partenaire en 2010.

Frais d'établissement

Les frais d'établissement correspondent aux frais de constitution et de premier établissement de la Société, et sont complètement amortis.

Logiciels et brevets

Les immobilisations incorporelles incluent des logiciels informatiques, un portefeuille de brevets acquis au cours de l'exercice 2009 et intégralement déprécié depuis 2020.

Les sommes versées pour l'acquisition de droits incorporels sont inscrites à l'actif dès lors que ces droits constituent une source de profits futurs probables, et sont dotés d'une pérennité suffisante. Un test de dépréciation est réalisé dès lors qu'il existe un indice de perte de valeur des actifs incorporels.

Les immobilisations incorporelles sont évaluées à leur coût d'acquisition. Leur amortissement est calculé selon la méthode linéaire sur leur durée probable de vie économique, selon les modalités suivantes :

Logiciels, concessions	3 à 5 ans

1.2.2 - Immobilisations corporelles

Les immobilisations corporelles sont évaluées à leur coût d'acquisition, les coûts d'acquisition sont inclus dans la valeur brute. Leur amortissement est calculé selon la méthode linéaire sur leur durée probable de vie économique, selon les modalités suivantes :

Agencements et installations divers	10 ans
Matériel informatique	3 à 5 ans
Mobilier	10 ans

Le mode d'amortissement reflète le rythme de consommation des avantages économiques des immobilisations en fonction de leur utilisation probable.

1.2.3 - Immobilisations financières

Les immobilisations financières sont constituées de dépôts et cautionnements divers, de titres de participation dans les filiales de la Société, ainsi que d'actions propres et liquidités liées au contrat de liquidités.

Les titres de participation sont inscrits au bilan à leur coût d'acquisition hors frais d'acquisition. Cette valeur est comparée en fin de période à la valeur d'usage de ces mêmes titres correspondant à la valeur la plus élevée entre la quote-part des capitaux propres correspondant à la participation et les flux de trésorerie actualisés basés sur des perspectives de rentabilité nécessitant l'utilisation d'hypothèses, d'estimations ou d'appréciations. Une provision est constatée lorsque la valeur d'usage est inférieure au coût d'acquisition.

Les immobilisations financières comprennent les actions propres et des espèces détenues dans une perspective de régulation de cours et d'amélioration de la liquidité des transactions. Ces opérations sont effectuées dans le cadre d'un contrat de liquidité signé avec la société Kepler-Chevreux et conformément à l'Assemblée Générale du 16 Juin 2020. Le Conseil d'Administration a décidé, dans sa séance du 16 Juillet 2020, d'utiliser l'autorisation donnée par l'Assemblée Générale du 20 Juin 2020 en vue de l'animation du marché secondaire ou la liquidité des actions de la société, par intervention systématique en contre tendance sur le marché et exclusivement dans le cadre du contrat de liquidité signé avec Kepler-Cheveux. Elles sont valorisées au coût d'achat. Une provision pour dépréciation est constatée sur les actions propres lorsque le cours moyen de clôture du dernier mois de l'exercice est inférieur au prix d'achat.

1.2.4 - Créances

Elles sont prises en compte pour leur valeur historique. Elles sont le cas échéant dépréciées pour tenir compte des risques de non-recouvrement.

1.2.5 - Crédit d'impôt recherche

Le Crédit d'Impôt Recherche (CIR) est accordé aux entreprises par les autorités fiscales françaises dans le but de les encourager à mener des recherches techniques et scientifiques. Les entreprises qui sont en mesure de démontrer qu'elles engagent des dépenses de recherche répondant aux critères du CIR bénéficient d'un crédit d'impôt qui peut être utilisé pour le paiement de leur impôt sur le revenu de l'exercice au cours duquel les dépenses ont été engagées, et pendant les trois exercices suivants. Si les impôts dus ne suffisent pas à couvrir le montant total du crédit d'impôt à la fin de la période de trois ans, la différence est remboursée à la Société en liquidités par les autorités fiscales françaises. La Société répond également à certains critères qui la font entrer dans la catégorie des petites et moyennes entreprises, ce qui lui permet de demander un paiement immédiat du CIR. Les dépenses prises en compte dans le calcul du CIR ne comprennent que les dépenses consacrées à la recherche.

Les dépenses de recherche et développement engagées par la Société Nicox S.A., ouvrent droit, sous certaines conditions, à un crédit d'impôt recherche égal à 30% des dépenses de recherche éligibles engagées au cours de l'année. Le crédit d'impôt est imputable sur l'impôt sur les sociétés dû par l'entreprise au titre de l'année au cours de laquelle elle a engagé ses dépenses de recherche. Le crédit excédentaire non imputé constitue une créance sur l'Etat qui peut être utilisée pour le paiement de l'impôt dû au titre des trois années suivantes celle au titre de laquelle elle est constatée. La fraction non utilisée à l'expiration de cette période est remboursée. Au cours du mois de décembre 2010 une disposition fiscale de la Loi de finance 2011 a été adoptée afin de permettre aux PME de demander le remboursement anticipé du crédit d'impôt recherche l'année suivant la constatation de la créance lorsque le crédit d'impôt n'est pas utilisable pour le paiement de l'impôt sur les sociétés

Au 31 décembre 2022, la Société a reçu le remboursement de son crédit d'impôt recherche 2020 et 2021 sur l'année, d'un montant respectif de 735 673€ et 716 324€.

1.2.6 – Trésorerie et équivalents de trésorerie

Les dépôts liquides et à court terme figurant dans l'état de la situation financière regroupent les disponibilités en banque et en caisse, ainsi que les dépôts à court terme assortis d'une échéance inférieure à six mois, qui sont soumis à un faible risque de changement de valeur.

1.2.7 - Conversion des éléments en devises

Les opérations en monnaies étrangères sont initialement enregistrées dans la monnaie fonctionnelle au taux de change en vigueur à la date de la transaction. Les actifs et passifs monétaires libellés en monnaies étrangères sont convertis aux cours de change en vigueur à la date de clôture. Les différences de change qui résultent des opérations précitées sont inscrites à l'actif et au passif en écart de conversion. En cas de pertes latentes (écarts de conversion actifs), une provision pour risque de change est constituée. Conformément aux règles comptables de prudence, les profits de change latents (écarts de conversion passifs) ne sont pas comptabilisés en résultat.

La Société n'a pas utilisé d'instrument de couverture pour couvrir son risque devise.

1.2.8 - Provisions

Les provisions correspondent aux engagements résultant de litiges et risques divers, dont l'échéance ou le montant sont incertains, auxquels la Société peut être confrontée dans le cadre de ses activités. Une provision est comptabilisée lorsque la Société a une obligation juridique ou implicite envers un tiers résultant d'un événement passé, dont il est probable ou certain qu'elle provoquera une sortie de ressources au bénéfice de ce tiers, sans contrepartie au moins équivalente attendue de celui-ci, et que les sorties futures de liquidité peuvent être estimées de manière fiable.

Les passifs éventuels ne sont pas comptabilisés mais font l'objet d'une information dans les notes annexes sauf si la probabilité d'une sortie de ressources est très faible.

1.2.9 - Engagement de retraite envers le personnel

Les engagements de la Société résultant de régimes de retraite à prestations définies sont déterminés en utilisant la méthode actuarielle des unités de crédit projetées, en application de la recommandation ANC 2013-02. Ces régimes ne sont pas financés. L'évaluation de ces engagements a lieu à chaque date de clôture. Les hypothèses actuarielles utilisées pour déterminer les engagements tiennent compte des conditions économiques prévalant dans le pays. Les engagements de la Société sont inscrits au passif du bilan. Les éventuels écarts actuariels sont comptabilisés en charge au cours de l'exercice. L'option d'étalement des coûts retenue est l'étalement sur les dernières années de carrière.

Les engagements de retraite à prestations définies s'élèvent au 31 décembre 2022 à 577 729€ contre 660 703€ au 31 décembre 2021.

Certains avantages sont également fournis par des régimes à cotisations définies dont les cotisations sont inscrites en charges lorsqu'elles sont encourues.

Les hypothèses utilisées pour calculer ces engagements sont précisées dans le tableau ci-dessous :

	Au 31 décembre	
	2022	**2021**
Taux d'actualisation [(1)]	3.70%	0.88%
Augmentations futures des salaires	2.5%	2%
Tables de mortalité	INSEE 2015	INSEE 2015

(1) Source : E Corp.AA supérieur à 10 ans.

1.2.10 - Evénements postérieurs à la clôture

Les états financiers de la Société sont ajustés pour refléter des mouvements ultérieurs relatifs à des conditions existantes à la date de clôture.

Ces ajustements ont lieu jusqu'à la date d'arrêté des comptes par le Conseil d'administration.

Les autres événements postérieurs à la date de clôture ne donnant pas lieu à des ajustements sont présentés dans les notes.

1.2.11 - Eléments du compte de résultat

- Produits d'exploitation générés par les accords de licence et de développement

Les produits d'exploitation de la société proviennent de royalties perçues sur les ventes d'un candidat médicament et d'un accord de licence exclusif sur le marché chinois pour le développement et la commercialisation d'un autre candidat médicament.

- Charges d'exploitation

La Société sous-traite ses activités de recherche et développement à des partenaires externes. En comptabilité, la Société enregistre ces dépenses en fonction de l'avancement des travaux. Le degré d'avancement est déterminé sur la base des informations communiquées par les partenaires externes, corroborées par des analyses internes.

Les redevances à verser à Pfizer par Nicox dans le cadre du contrat de rachat de droits du latanoprostène bunod (désormais VYZULTA) par Nicox en 2009 sont reconnues dès lors que les ventes sur lesquelles ces royalties sont calculées, sont réalisées par Bauch & Lomb, partenaire auprès duquel VYZULTA a été licencié en 2010.

1.2.12 – Emprunt

Les emprunts sont comptabilisés au passif pour leur valeur totale, prime de remboursement incluse.
La prime de remboursement des obligations est amortie en linéaire sur la durée de l'emprunt, c'est-à-dire par fractions égales au prorata de la durée de l'emprunt.

2. COMPLEMENTS D'INFORMATION RELATIFS AU BILAN ET AU COMPTE DE RESULTAT

2.1 Immobilisations incorporelles et amortissements

Immobilisations incorporelles en Euros	31.12.21	Acquisitions	Cessions et mises au rebut	Autres	31.12.22
Frais d'établissement	58 278	-	-	-	58 278
Frais de recherche développement	50 000	-	-	-	50 000
Concessions, brevets, droits similaires et logiciels	2 819 315	-	-	-	2 819 315
Total des immobilisations incorporelles	**2 927 593**	**-**	**-**	**-**	**2 927 593**

Amortissement et dépréciations des immobilisations incorporelles en Euros	31.12.21	Dotations	Cessions et mises au rebut	31.12.22
Frais d'établissement	58 278	-	-	58 278
Frais de recherche développement	50 000	-	-	50 000
Concessions, brevets, droits similaires et logiciels	236 941	301	-	237 242
Provision pour dépréciation des Concessions, brevets, droits similaires et logiciels	2 581 240	-	-	2 581 240
Total amortissement et dépréciations des immobilisations incorporelles	**2 926 459**	**301**	**-**	**2 926 760**

2.2 Immobilisations corporelles et amortissements

Immobilisations corporelles en Euros	31.12.21	Acquisitions	Cessions et mises au rebut	Autres	31.12.22
Installations générales, agencements	224 517	8 030	-	-	232 547
Matériel de bureau, informatique, mobilier, véhicules	503 472	19 263	-	-	522 735
Total des immobilisations corporelles	**727 989**	**27 293**	**-**	**-**	**755 282**

Amortissement et dépréciations des immobilisations corporelles en Euros	31.12.21	Dotations	Cessions et mises au rebut	31.12.22
Amortissements Installations générales, agencements	224 453	201	-	224 653
Amortissement Matériel de bureau, informatique, mobilier	493 135	12 178	-	505 313
Total amortissement des immobilisations corporelles	**717 588**	**12 378**	**-**	**729 966**

2.3 Immobilisations financières & dépréciations

Les immobilisations financières sont composées de dépôts et cautionnements relatifs au bail des bureaux de la Société, des dépôts concernant le prêt Kreos, de titres de participation de la Société Nicox dans ses filiales et d'actions auto-détenues.

Immobilisations financières en Euros	31.12.21	Augmentations	Diminutions	31.12.22
Dépôts & cautionnements	679 579	1 119	31 977	648 721
Titres de participations (1)	55 631 553	-	-	55 631 552
Autres immobilisations financières (2)	693 947		348 491	345 456
Sous total des immobilisations financières	**57 005 079**	**1 119**	**380 468**	**56 625 729**

(1) Les titres de participations s'élèvent à 55 631 552€ et correspondent à la participation de la Société dans sa filiale italienne pour 1 009 760€ et 54 621 792€ dans sa filiale américaine.
(2) Correspond au contrat de liquidité signé avec la société Kepler-Cheveux

Dépréciations financières en Euros	31.12.21	Dépréciations	Annulation dépréciations	31.12.22
Dépréciation des titres de participation Nicox Ophthalmics (1)	40 200 037	11 500 000	-	51 700 037
Total des dépréciations financières	**40 200 037**	**11 500 000**	**-**	**51 700 037**

(1) Correspond à la dépréciation des titres de participation dans la filiale US. Il a été constaté des pertes de valeurs des actifs incorporels de la filiale US, Nicox Ophthalmics Inc. C'est pourquoi il a été décidé de déprécier ces actifs dans les comptes de la Société en 2021 à hauteur de 12 700 000€ pour le ZERVIATE et 15 100 000€ pour le NCX4251. Aussi, une dotation complémentaire relative au NCX4251 de 11 500 000€ a été constatée en 2022 suite à la décision du Groupe de chercher un partenaire pour poursuivre le développement du produit sur le marché américain. Cette dotation est enregistrée en Dotations financières aux amortissements et provisions.

2.4 Echéance des créances à la clôture de l'exercice

Le tableau des créances est présenté ci-dessous avec mention des échéances :

Créances (montants en Euros)	Total	A moins d'un an	A plus d'un an
Avances et acomptes	194 423	194 423	-
Créances clients	2 623 378	2 623 378	-
Autres créances	64 533	64 533	-
Etat, taxe sur la valeur ajoutée	149 802	149 802	-
Etat, Crédit d'Impôt Recherche (CIR) et Taxe sur salaires (1)	1 290 264	516 038	774 226
Créances sur filiale (2)	36 145 208	10 905	36 134 303
Charges constatées d'avance	1 480 416	1 480 416	-
Total créances	**41 948 024**	**5 039 495**	**36 908 529**

(1) Comprend entre autres le CIR 2022 pour 504 372€, et la contestation du redressement fiscal pour 774 226€

(2) Comprend le compte courant de la filiale américaine, Nicox Ophthalmics, Inc. au 31/12/22 pour 36 134 303€.

2.5 Disponibilités

Les disponibilités s'élèvent à 27 079 935 € au 31 décembre 2022 dont 16 597 269€ sont investies en comptes à terme, convertibles en un montant connu de trésorerie et sans risque de changement de valeur, le capital étant garanti.

Au 31 décembre 2022, les intérêts courus à recevoir s'élèvent à 17 719€.

2.6 Charges constatées d'avance

Les charges constatées d'avance se répartissent selon le tableau suivant :

Charges constatées d'avance en Euros	Au 31 décembre 2022
Assurances	7 230
Frais de développement	1 317 558
Honoraires Consultants	114 143
Divers	41 485
Total charges constatées d'avance	**1 480 416**

2.7 Prime de remboursement des obligations.

La prime de remboursement porte sur l'emprunt obligataire non convertible de Kreos dont la valeur nominale s'élève à 1 787 000€ et pour lequel une prime est due à l'échéance (1er janvier 2026) pour 2 466 538€.
Cette prime est amortie prorata temporis sur la durée de l'emprunt. Sa valeur nette s'élève à 1 826 571€ au 31 décembre 2022. Cf les modalités d'amortissement de la prime en 1.2.12.

2.8 Capitaux propres

2.8.1 - Généralités

Au 31 Décembre 2022 le capital social est composé de 50 100 448 actions ordinaires de 1€ de valeur nominale entièrement libérées.

Par ailleurs, la Société détient au 31 Décembre 2022, 288 965 actions propres au cours de 1.12€, soit une valeur totale de 323 641€.

Capital Autorisé

	Au 31 décembre	
	2022	**2021**
Le capital est constitué d'actions de valeur nominale 1€	50 100 448	43 138 185

Au cours de l'année 2022, Nicox SA a procédé à diverses augmentations de capital par émission d'actions gratuites pour un montant total de 112 947€ et par une émission de 6 849 316 actions ordinaires nouvelles.

Le tableau de variation des capitaux propres est présenté ci-dessous :

	Actions ordinaires		Primes liées au capital	Pertes cumulées	Total des capitaux propres
	Nombre	Montant			
Au 31 Décembre 2021	**43 138 185**	**43 138 185**	**527 545 675**	**(506 069 209)**	**64 614 651**
Émission d'actions ordinaires par voie d'instruments de Capitaux Propres	6 849 316*	6 849 316	2 114 385	-	8 963 701
Émission d'actions Gratuites	112 947	112 947	(112 947)	-	-
Résultat de l'exercice	-	-	-	(31 284 980)	(31 284 980)
Au 31 Décembre 2022	**50 100 448**	**50 100 448**	**529 547 113**	**(537 354 189)**	**42 293 374**

*Augmentation de capital sans droit préférentiel de souscription réservée à la souscription de sociétés ou fonds gestionnaires d'épargne collective de droit français ou de droit étranger investissant dans le secteur pharmaceutique/biotechnologique. Cette augmentation de capital a donné lieu à l'émission de 6 849 316 actions ordinaires nouvelles assorties chacune d'un bon de souscription d'actions portant globalement sur 6 849 316 nouvelles actions ordinaires supplémentaires pour un montant brut de 10 millions d'euros

2.8.2 - Options de souscription d'actions

Le 22 octobre 2014, l'Assemblée Générale des actionnaires a approuvé un plan d'options de souscription d'actions au bénéfice des salariés et mandataires sociaux du Groupe et a autorisé le Conseil d'administration à octroyer des options donnant droit de souscrire un nombre maximum de 200 000 actions ordinaires (entendu après regroupement des actions survenu le 3 décembre 2015), existantes ou nouvelles, d'une valeur nominale de € 1. L'acquisition définitive de ces options est soumise à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits. Le Conseil d'administration détermine l'identité des bénéficiaires des attributions ainsi que les conditions et les critères d'attribution des options. Les options attribuées sous cette autorisation devraient être exercées au plus tard 6 ans après la date de leur attribution effective par le Conseil d'administration. Cette autorisation, consentie pour une durée de 38 mois à compter de la date de l'assemblée, a été privée d'effet par l'Assemblée Générale des actionnaires du 3 juin 2015 mais aucune option n'a été attribuée sous autorisation de cette assemblée générale.

Le 24 mai 2018, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, 1,000,000 options de souscription ou d'achat d'actions. L'exercice de ces options est soumis, s'agissant des bénéficiaires qui sont membres du Comité de direction, à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits. Les options attribuées sous cette autorisation devraient être exercées au plus tard 8 ans après la date de leur attribution effective par le Conseil d'administration. Cette autorisation, consentie pour une durée de 38 mois à compter de la date de l'assemblée, a été privée d'effet par l'Assemblée Générale des actionnaires du 30 juin 2020.

Le 30 juin 2020, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, 1,000,000 options de souscription ou d'achat d'actions. L'exercice de ces options est soumis, s'agissant des bénéficiaires qui sont membres du Comité de direction, à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits. Les options attribuées sous cette autorisation devraient être exercées au plus tard 8 ans après la date de leur attribution effective par le Conseil d'administration.

Le 28 avril 2021, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, 2 500 000 options de souscription ou d'achat d'actions. L'exercice de ces options est soumis, s'agissant des bénéficiaires qui sont membres du Comité de direction, à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des

droits. Les options attribuées sous cette autorisation devraient être exercées au plus tard 8 ans après la date de leur attribution effective par le Conseil d'administration.

Le 28 juillet 2022, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, 2 500 000 options de souscription ou d'achat d'actions. L'exercice de ces options est soumis, s'agissant des bénéficiaires qui sont membres du Comité de direction, à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits. Les options attribuées sous cette autorisation devraient être exercées au plus tard 8 ans après la date de leur attribution effective par le Conseil d'administration.

Les options de souscription d'actions attribuées entre le 1er janvier 2015 et le 31 décembre 2021 étaient soumises à des conditions de performance d'atteinte de 70% et ces conditions ont toujours été atteintes. A partir de janvier 2022 la performance d'atteinte de l'objectif est passé à 50%.

Options en circulation au 31.12.2022

Date du Conseil d'Administration	Options attribués	Point de départ de l'exercice des options	Date d'expiration	Prix de souscription par option en euros	Nombre d'options annulées ou expirées	Options en circulation	Nombre d'actions en circulation à émettre par exercice des options
Plan autorisé par l'Assemblée générale du 22/10/2014							
30/01/2015	200 000	30/01/2019	30/01/2021	1.8700 €	200 000	0	0
	200 000				**200 000**	**0**	**0**
Plan autorisé par l'Assemblée générale du 24/05/2018							
12/02/2019	176 550	12/02/2021	12/02/2027	6.0546 €	54 150	122 400	122 400
27/01/2020	394 750	27/01/2022	27/01/2028	4.7910 €	84 600	310 150	310 150
	571 300				**138 750**	**432 550**	**432 550**
Plan autorisé par l'Assemblée générale du 30/06/2020							
15/10/2020	56 000	31/10/2021	15/10/2028	2.9200 €	40 000	16 000	16 000
15/10/2020	56 000	31/10/2022	15/10/2028	2.9200 €	40 000	16 000	16 000
14/01/2021	349 550	14/01/2023	14/01/2029	3.5181 €	56 000	293 550	293 550
	461 550				**136 000**	**325 550**	**325 550**
Plan autorisé par l'Assemblée générale du 28/04/2021							
15/02/2022	457 500	15/02/2024	15/02/2030	2.3716 €	47 700	409 800	409 800
07/04/2022	52 000	08/04/2022	07/04/2030	2.9200 €	36 000	16 000	16 000
07/04/2022	52 000	31/10/2022	07/04/2030	2.9200 €	36 000	16 000	16 000
07/04/2022	33 300	14/01/2023	07/04/2030	3.5181 €	24 300	9 000	9 000
01/07/2022	286 666	01/06/2023	01/07/2030	1.7954 €	0	286 666	286 666
01/07/2022	286 666	01/06/2024	01/07/2030	1.7954 €	0	286 666	286 666
01/07/2022	286 668	01/06/2025	01/07/2030	1.7954 €	0	286 668	286 668
19/07/2022	328 673	19/07/2023	18/07/2030	1.7965 €	36 668	292 005	292 005
19/07/2022	328 664	19/07/2024	18/07/2030	1.7965 €	36 666	291 998	291 998
19/07/2022	15 000	19/07/2024	18/07/2030	1.7965 €	5 000	10 000	10 000
19/07/2022	328 663	19/07/2025	18/07/2030	1.7965 €	36 666	291 997	291 997
	2 455 800				**259 000**	**2 196 800**	**2 196 800**
Plan autorisé par l'Assemblée générale du 28/07/2022							
23/09/2022	28 670	23/09/2023	23/09/2030	1.9000 €	0	28 670	28 670
23/09/2022	28 665	23/09/2024	23/09/2030	1.9247 €	0	28 665	28 665
23/09/2022	28 665	23/09/2025	23/09/2030	1.9247 €	0	28 665	28 665
	86 000				**0**	**86 000**	**86 000**
	3 774 650				733 750	3 040 900	3 040 900

Le tableau suivant illustre le nombre et les prix moyens pondérés d'exercice des options proposées par le plan :

	Au 31 décembre 2022		
	Nombre d'options	**Nombre d'actions**	**Moyenne pondérée des prix d'exercice des actions correspondantes aux options (en euros)**
Options en circulation en début de période	**904 250 ***	**904 250 ***	**4.33**
Attribuées pendant la période	2 541 800	2 541 800	1.97
Annulées	(405 150)	(405 150)	2.92
En circulation à la fin de la période	**3 040 900**	**3 040 900**	**2.55**

* 137 300 options de souscription d'actions attribuées en 2020 et 2021 ont été annulées rétroactivement par le conseil d'administration du 07 avril 2022

La durée de vie contractuelle résiduelle moyenne pondérée pour les options en circulation est de 6 ans et 4 mois au 31 décembre 2022 (6 ans et 6 mois au 31 décembre 2021).

2.8.3 - Bons de souscription d'actions

2.8.3.1 BSA attribués aux administrateurs et au comité consultatif clinique

Le 30 mai 2017, l'Assemblée Générale des actionnaires a autorisé le principe d'une augmentation de capital d'un montant de € 144 000 par émission à titre gratuit de 144 000 bons de souscription d'actions donnant droit à un droit à un maximum de 144 000 nouvelles actions ordinaires d'une valeur nominale de € 1 au bénéfice de six membres du Conseil d'administration. Ces bons ont été émis par le Conseil d'administration le 8 juin 2017 et devront exercés dans un délai maximum de cinq ans à compter de leur émission. L'exercice de ces bons était soumis à des conditions de performance fixées par le Conseil au moment de l'attribution des droits dont l'atteinte a été constatée par le Conseil en décembre 2017. Ces bons de souscription ont expiré au cours de l'exercice 2022 (le 07 juin 2022) sans avoir pu être exercés.

Le 24 mai 2018, l'Assemblée Générale des actionnaires a autorisé le principe d'une augmentation de capital d'un montant de € 300 000 par émission à titre gratuit de 300 000 bons de souscription d'actions donnant droit à un droit à un maximum de 300 000 nouvelles actions ordinaires d'une valeur nominale de € 1 au bénéfice de six membres du Conseil d'administration alors en fonction (Madame Birgit Stattin Norinder ayant démissionné à effet du 20 juin 2018). 144 000 bons ont été émis par le Conseil d'administration le 25 mai 2018 et devront être exercés dans un délai maximum de cinq ans à compter de leur émission. L'exercice de ces bons était soumis à des conditions de performance fixées par le Conseil au moment de l'attribution des droits dont l'atteinte a été constatée par le Conseil en septembre 2018.

Le 30 juin 2020 l'Assemblée Générale des actionnaires a autorisé le principe d'une augmentation de capital d'un montant de € 60 000 par émission à titre gratuit de 60 000 bons de souscription d'actions (BSA) donnant droit à un maximum de 60 000 nouvelles actions ordinaires d'une valeur nominale de € 1 au bénéfice des six membres du comité consultatif clinique sur le glaucome constitué par la Société. L'exercice de ces bons était soumis à des conditions de performance fixées par le Conseil au moment de l'attribution des droits dont l'atteinte a été constatée par le Conseil en septembre 2020.

Le tableau suivant présente, au 31 décembre 2022, les bons de souscription d'actions en circulation :

	Plan n°7	Plan n°8	Plan n°9
Date d'assemblée	Mai 2017	Mai 2018	Juin 2020
Date du Conseil d'administration	8 juin 2017	25 mai 2018	16 juillet 2020
Nombre total d'actions pouvant être souscrites	144 000	144 000	60 000
Date d'expiration	7 juin 2022	24 mai 2023	15 juillet 2025
Prix de souscription d'une action sur exercice d'un bon (€)	11,8841	8,8803	4,1449
Modalités d'exercice (lorsque le plan comporte plusieurs tranches)	(1)	(1)	
Nombre d'actions souscrites au 31 décembre 2022		-	-
Nombre cumulé de bons de souscription d'actions annulées ou caduques	144 000	-	-
Bons de souscription d'actions restants en fin d'exercice	0	144 000	60 000

(1) L'exercice des bons est subordonné à ce que le Conseil ait constaté la réalisation de certains objectifs stratégiques non divulgués, ce qui a été le cas.

Le tableau suivant illustre le nombre et les prix moyens pondérés d'exercices proposés par le plan :

	Au 31 décembre 2022		
	Nombre d'options	**Nombre d'action**	**Moyenne pondérée des prix d'exercice des options en euros**
En circulation en début de période	**348 000**	**348 000**	**9.31**
Attribués pendant la période	-	-	-
Annulées ou caduques pendant la période	(144 000)	(144 000)	11.88
En circulation à la fin de la période	204 000	204 000	7.49
Exerçables à la fin de la période	**204 000**	**204 000**	**7.49**

2.8.3.2 Bons de souscriptions d'actions attribués aux investisseurs et créanciers

Le tableau ci-dessous présente les bons de souscriptions d'actions attribués à des investisseurs lors de levées de fonds ainsi qu'à Kreos dans le cadre du contrat de prêt en vigueur avec la Société. L'ensemble de ces bons est en circulation au 31 décembre 2022 et aucune annulation ou expiration n'est intervenue depuis leur attribution. Par ailleurs la levée de fonds de 2022 est assortie d'une option de vente des bons de souscription d'actions au bénéfice d'Armistice telle que décrite en note 2.18.2.5

	Date d'attribution	Droits	Nombre d'actions à emettre	Date d'expiration	Prix d'exerice
Prêt Kreos	23-janv.-19	308 848	308 848	23-janv.-24	€5,99
Prêt Kreos	28-févr.-21	100 000	100 000	28-févr.-26	€4,23
Placement privé 2021	13-déc.-21	6 018 000	5 100 000	13-déc.-26	€3,21
Placement privé 2022	21-nov.-22	6 849 316	6 849 316	21-nov.-27	€1,70

2.8.3.3 Obligations convertibles en actions.

Le prêt convertible de 3 300 000€ de Kreos donne droit à l'émission de 900 000 actions au prix de conversion de 3.67€ et sont convertibles à échéance du 1 er janvier 2026 (Cf note 2.10).

2.8.4 - Actions gratuites

Le 24 mai 2018, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, à titre gratuit, des actions existantes ou à émettre du groupe dans la limite de 1 000 000 actions ordinaires existantes ou nouvelles, d'une valeur nominale de 1€. L'acquisition définitive de ces actions est soumise à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits.

L'acquisition des actions gratuites attribuées en 2018 en vertu du plan autorisé le 24 mai 2018 était subordonnée, pour certains droits, à ce que le Conseil d'administration constate la réalisation des objectifs annuels du Groupe à hauteur au moins de 70% de réalisation. En janvier 2019, le Conseil d'administration a constaté que les objectifs non divulgués du Groupe avaient été remplis à hauteur de 90%.

L'acquisition des actions gratuites attribuées en 2019 en vertu du plan autorisé le 24 mai 2018 était subordonnée, pour certains droits, à ce que le Conseil d'administration constate la réalisation des objectifs annuels du Groupe à hauteur au moins de 70% de réalisation. En mars 2020 le Conseil d'administration a constaté que les objectifs non divulgués du Groupe avaient été remplis à hauteur de 90%.

L'acquisition des actions gratuites attribuées en 2020 en vertu du plan autorisé le 30 mai 2017 était subordonnée à ce que le Conseil d'administration constate la réalisation des objectifs annuels du Groupe à hauteur au moins de 70% de réalisation. En décembre 2020, le Conseil d'administration a constaté que les objectifs non divulgués du Groupe avaient été remplis à hauteur de 100%.

Le 28 avril 2021, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, à titre gratuit, des actions existantes ou à émettre du groupe dans la limite de 1 000 000 actions ordinaires existantes ou nouvelles, d'une valeur nominale de € 1. L'acquisition définitive de ces actions est soumise à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits.

L'acquisition des actions gratuites attribuées en 2021 en vertu du plan autorisé le 28 avril 2021 était subordonnée, pour certains droits, à ce que le Conseil d'administration constate la réalisation des objectifs annuels du Groupe à hauteur au moins de 70% de réalisation. En décembre 2021 le Conseil d'administration a constaté que les objectifs non divulgués du Groupe avaient été remplis à hauteur de 70%.

Le 28 juillet 2022, l'Assemblée Générale des actionnaires a autorisé le Conseil d'administration, pour une durée de 38 mois, à attribuer aux salariés et mandataires sociaux du Groupe, à titre gratuit, des actions existantes ou à émettre du groupe dans la limite de 1 000 000 actions ordinaires existantes ou nouvelles, d'une valeur nominale de € 1. L'acquisition définitive de ces actions est soumise à des conditions de performance fixées par le Conseil d'administration au moment de l'attribution des droits.

L'acquisition des actions gratuites attribuées en 2022 en vertu du plan autorisé le 14 septembre 2022 était subordonnée, pour certains droits, à ce que le Conseil d'administration constate la réalisation des objectifs annuels du Groupe à hauteur au moins de 50% de réalisation. En janvier 2023, le Conseil d'administration a constaté que les objectifs non divulgués du Groupe avaient été remplis à hauteur de 100%.

Le tableau suivant présente, au 31 décembre 2022, les actions gratuites en circulation émises dans le cadre de ces plans :

Date du Conseil d'Administration	Actions attribués	Date d'acquisition des actions	Nombre d'actions annulées	Actions acquises	Total à émettre
Plan autorisé par l'Assemblée générale du 24/05/2018					
12/02/2019	83 650	12/02/2021	10 000	73 650	0
19/04/2019	8 000	19/04/2021	0	8 000	0
24/05/2019	1 400	24/05/2021	0	1 400	0
11/07/2019	12 000	11/07/2021	0	12 000	0
16/09/2019	12 800	16/09/2021	0	12 800	0
27/01/2020	99 750	27/01/2022	14 800	84 950	0
05/03/2020	8 000	05/03/2022	8 000	0	0
05/08/2020	24 000	05/08/2022	12 000	12 000	0
15/10/2020	54 000	15/10/2022	38 003	15 997	0
	303 600		**82 803**	**220 797**	**0**
Plan autorisé par l'Assemblée générale du 30/06/2020					
14/01/2021	83 150	14/01/2023	26 900	0	56 250
	83 150		**26 900**	**0**	**56 250**
Plan autorisé par l'Assemblée générale du 28/04/2021					
05/05/2021	13 800	05/05/2023	0	0	13 800
19/07/2021	2 400	19/07/2023	2 400	0	0
16/12/2021	9 000	16/12/2023	9 000	0	0
12/01/2022	33 700	12/01/2024	11 500	0	22 200
15/02/2022	129 600	15/02/2024	16 000	0	113 600
19/07/2022	725 400	19/07/2024	56 000	0	669 400
	913 900		**94 900**	**0**	**819 000**
Plan autorisé par l'Assemblée générale du 28/07/2022					
23/09/2022	71 000	23/09/2024	0	0	71 000
	71 000		**0**	**0**	**71 000**
	1 371 650		204 603	220 797	946 250

2.9 Provisions pour risques et charges

Le tableau des provisions inscrites au bilan est présenté ci-dessous :

Provisions inscrites au bilan en Euros	**31.12.21**	**Dotations**	**Reprises sur Provisions**	**31.12.22**
Provision pour risque, ainsi que pertes de change- comptes en devises (1)	**3 030**	**38 724**	**3 030**	**38 724**
Provision pour indemnité fin de carrière	**660 703**	**4 667**	**87 641**	**577 729**
Total des provisions pour risques et charges	**663 733**	**43 391**	**90 671**	**616 453**

(1) Ce montant correspond à la réévaluation des fournisseurs en USD au taux de clôture du 31/12/2022

2.10 Échéances des dettes à la clôture de l'exercice

Nicox a conclu avec Kreos Capital un contrat de financement d'un montant de 20 millions d'euros, structuré en 3 tranches d'obligations garanties de premier rang, Ces tranches ont été versées entre le 1er février 2019 et le 2 janvier 2020. En janvier 2021, Nicox a amendé l'accord de financement obligataire avec Kreos Capital pour introduire une période supplémentaire d'une année, à compter du 1er février 2021, durant laquelle le remboursement a été limité aux seuls intérêts portant sur le principal restant dû et a étendu la durée du prêt de 6 mois jusqu'en juillet 2024. Ce report concernait les trois tranches de l'emprunt et prévoyait un remboursement sur le même calendrier de paiement.

Un nouvel amendement à l'accord de financement obligataire a été signé le 30 novembre 2021. A cette date, le montant du capital restant dû s'élevait à 16,9 millions, montant qui incluait 0,6 million d'euros prépayés lors de l'appel des tranches. Ces 0,6 million correspondent aux dernières échéances de paiement du capital pour chacune des tranches appelées. Par cet amendement, la période durant laquelle seuls les intérêts sont payés a été étendue de 18 mois jusqu'en juillet 2023 (contre janvier 2022 précédemment) et la date d'échéance du prêt a été reportée de 18 mois jusqu'au 1er janvier 2026. Cet amendement incluait également une option d'extension de la période durant laquelle seuls les intérêts sont payés et une extension de la durée du prêt de six mois supplémentaires en fonction d'objectifs portant sur l'étude de phase 3 Mont Blanc sur le NCX 470. Ces modifications se sont appliquées à 70 % du capital restant dû, hors acompte de 0,6 million d'euros (le « Prêt à Terme »). Le taux d'intérêt de 9,25 % est resté inchangé. En échange de l'extension de la période de remboursement de 18 mois supplémentaire de paiement des seuls intérêts sur le « prêt à terme », 3.3 millions d'euros du capital restant avant l'amendement ont été émis sous forme d'obligations convertibles (le « Prêt Convertible »). Ce prêt convertible est à échéance du 1er janvier 2026, avec le même taux d'intérêt de 9,25 % par an, payable en numéraire. Le Prêt Convertible est garanti par les sûretés en place pour le Prêt à Terme. Cette partie de la dette peut être convertie en actions à la discrétion de Kreos à tout moment (après une période initiale de 60 jours) et ce jusqu'à la date d'échéance du 1er janvier 2026. Le prix de conversion est de 3,67 euros. Si Kreos n'a pas converti les obligations à l'échéance du Prêt Convertible, le montant total du Prêt Convertible sera alors intégralement dû en un seul versement. Si Kreos convertit les obligations, les actionnaires existants s'en trouveraient diluées.

Les 1,8 millions d'euros restants ont été émis sous forme de nouvelles obligations non convertibles avec un taux d'intérêt de 9,25 %, pour une durée identique à celle du prêt convertible et avec une prime supplémentaire payable au moment du remboursement égale à 1,75 fois le montant initial déduction faite des intérêts déjà payés sur la période.

En novembre 2022 la Société a exercé l'option lui permettant d'étendre pour 6 mois supplémentaires la période de paiement des seuls intérêts et la date d'échéance du prêt, soit respectivement jusqu'en janvier 2024 et juillet 2026, l'étude clinique de phase 3 Mont Blanc sur le NCX 470 ayant atteint son critère d'évaluation principal de non-infériorité par rapport au latanoprost avant le 1er juillet 2023. Cette option ne s'applique pas aux obligations convertibles pour un montant nominal de 3,3 millions d'euros ni aux obligations non convertibles pour un montant nominal de 1,8 millions d'euros dont l'échéance prime incluse reste le premier janvier 2026.

L'extension a permis de reporter le remboursement du capital dû pour la période du 1er août 2023 au 1er février 2024 d'un montant de 2,1 millions d'euros. Le remboursement s'effectuera du 1er février 2024 au 1er juillet 2026. Cette option d'extension du prêt de six mois supplémentaires a eu pour conséquence un paiement d'intérêts additionnel de 0,8 million d'euros en 2026.

Le contrat prévoit divers cas de d'échéance du terme de l'emprunt, en particulier la violation d'une obligation matérielle du contrat telle que le paiement des sommes dues ou le défaut de transmission d'informations financières ; le défaut de paiement d'une dette supérieure à € 150 000; l'ouverture d'une procédure judiciaire ou une cessation d'activité ; le changement de contrôle (en cas d'exercice de l'option de vente). Dans les cas de déchéance du terme prévus au contrat, les sommes dues au titre de l'emprunt deviendraient immédiatement remboursables et, à défaut de paiement, Kreos pourrait réaliser les sûretés. Il ne peut être garanti que Nicox disposera alors des ressources nécessaires pour faire face à un remboursement anticipé de l'emprunt souscrit.
La Société a consenti des sûretés sur certains de ses actifs corporels et incorporels, notamment des brevets relatifs au produit VYZULTA (le nantissement n'ayant pas d'impact sur le contrat de licence exclusif mondial conclu avec Bausch + Lomb), les titres de la filiale Nicox Ophthalmics, Inc. ainsi qu'un nantissement des comptes bancaires et de Risques liés à la fluctuation des revenus et des taux de changes, fiabilité des placements.

Le tableau des dettes est présenté ci-dessous avec mention des échéances :

Dettes en Euros	Total	A moins d'un an	Entre 1 et 5 ans	A + de 5 ans
Emprunt et dettes financières	**21 259 826**	495 951	20 763 875	
Dettes filiales et comptes courants d'actionnaires	**4 036 657**	-	4 036 657	
Fournisseurs & comptes rattachés	**2 537 119**	2 537 119		-
Dettes fiscales et sociales : Dettes envers le personnel	**563 748**	563 748		-
Organismes sociaux	**344 132**	344 132		-
Etat : Impôts et taxes à payer	**163 724**	163 724		-
Total des dettes	**28 905 206**	**4 104 674**	**24 800 532**	**-**

Le tableau relatif au poste « factures non parvenues » inclues dans la ligne Fournisseurs & comptes rattachés est présenté ci-dessous :

Fournisseurs factures non parvenues	Montants en Euros
Frais de développement	884 532
Frais généraux, divers	571 995
Honoraires consultants	186 393
Honoraires juridiques, comptables…	128 705
Total Fournisseurs factures non parvenues	**1 771 625**

Le tableau, ci-dessous, présente les charges à payer pour les postes « personnel charges à payer », « organismes sociaux » et « Etat : Impôts et taxes à payer » :

Charges fiscales et sociales à payer	Montants en Euros
Personnel, autres charges	61 126
Personnel, dettes provisionnées pour congés payés et primes à payer	563 748
Charges sociales provisionnées	247 259
Charges sociales à payer	35 747
Etat & autres charges à payer	163 724
Total des charges fiscales et sociales à payer	**1 071 604**

2.11 Produits constatés d'avance

Au 31 décembre 2022, la Société a constaté pour 2 169 171€ de produits constatés d'avance qui correspondent aux produits différés reconnus dans le cadre de l'amendement à l'accord de licence avec Ocumension sur l'étude NCX470 (voir note 2.17)

2.12 Écarts de conversion

L'écart de conversion passif d'un montant de 1 858 560€ correspond à la réévaluation du compte courant de la filiale américaine Nicox Ophthalmics Inc.

2.13 Autres achats et charges externes

Les charges d'exploitation de la Société comprennent les frais de Recherche & Développement pour un montant de 11 837 006€ au 31 décembre 2022 contre 8 844 210€ au 31 décembre 2021.

2.14 Reprises sur provisions et transferts de charges

Les reprises de provisions et transfert de charges s'élèvent à 96 594€ et correspondent essentiellement à la reprise de provision de l'indemnité de fin de carrière à la suite de l'évolution du taux d'actualisation.

2.15 Chiffre d'affaires et redevances pour concessions de brevet

Au 31 décembre 2022 le chiffre d'affaires se décompose comme suit :

Chiffre d'affaires et autres produits	
Refacturation aux filiales de la Société	211 624
Royalties perçues sur les ventes de VYZULTA [(1)]	5 241 677
Total	**5 453 301**

[(1)] Correspond aux redevances perçues sur les ventes de VYZULTA aux Etats-Unis licencié auprès de Baush & Lomb.

2.16 Autres charges

Les autres charges sont essentiellement constituées de paiements de redevances à Pfizer pour 1 970 573€ et des jetons de présence versés à nos cinq Administrateurs pour 250 000€.

Les redevances versées à Pfizer rémunèrent le rachat des droits du latanoprostène bunod sous forme d'un pourcentage des ventes versées par Bausch & Lomb.

2.17 Charges et produits financiers

Au 31 décembre 2022, les charges et produits financiers de Nicox S.A. s'analysent comme suit :

- **Produits financiers**

Produits financiers	**Montants en Euros**
Produits sur cession VMP	838
Autres intérêts et produits assimilés [(1)]	1 119 815
Différences positives de change	872 150
Reprises sur provisions	3 030
Total des produits financiers	**1 995 833**

[(1)] Les autres intérêts et produits assimilés incluent la refacturation d'intérêts sur comptes courants à la filiale américaine pour un montant de 557 559€ ainsi que des produits financiers sur des comptes à terme pour 519 514€.

- **Charges financières**

Charges financières	**Montants en Euros**
Dotations financières aux amortissements et provisions (1)	12 142 298
Intérêts et charges assimilés (2)	1 582 377
Différences négatives de change	401 012
Charges nettes sur cession de VMP (3)	348 851
Autres charges financières	48 486
Total des charges financières	**14 523 023**

(1) Correspond à la dotation complémentaire des titres de participation de la filiale américaine, Nicox Ophthalmics pour 11 502 331€ et à la dotation aux amortissements de la prime de remboursement des obligations Kreos pour 639 967€
(2) Correspond aux intérêts constatés au 31/12/22 sur l'emprunt Kreos.
(3) Correspond à la perte sur le placement des actions propres (Contrat Kepler)

2.18 Autres engagements financiers

2.18.1 Engagements donnés

A la connaissance de la Société, les engagements présentés décrits dans les paragraphes suivants, représentent l'intégralité des engagements hors bilan significatifs de la Société, ou qui pourraient le devenir dans le futur. Une synthèse de ces derniers est présentée dans les tableaux ci-après :

Obligations contractuelles	**Total**	**Paiements dus par période**		
		A moins d'un an	**D'un an à cinq ans**	**A plus de cinq ans**
Contrats de location locaux	99 129	56 645	42 484	-
Contrats de location véhicules	40 649	21 287	19 363	-
Engagements dans la Recherche et le développement	15 901 717	8 533 736	7 367 981	-
Accords de licences	14 063 379	-	14 063 379	-
Engagements de dettes financières	-	-	-	-
TOTAL	**30 104 874**	**8 611 668**	**21 493 206**	

La Société a également des engagements financiers associés au prêt Kreos, qui est garanti par des sûretés (cf. note 2.10).

2.18.2 Accords de licences

2.18.2.1 Ocumension

En décembre 2018, la Société, a conclu un accord de licence exclusif avec Ocumension Therapeutics une société internationale spécialisée en ophtalmologie. L'accord porte sur le développement et la commercialisation de son candidat médicament NCX 470 pour les patients atteints de glaucome ou d'hypertension oculaire sur un territoire comprenant la Chine continentale, Hong Kong, Macao et Taiwan. La

Société a concédé à Ocumension les droits exclusifs de développement et de commercialisation de NCX 470, à leurs frais, dans le territoire précité. Selon les termes de l'accord, la Société a reçu en décembre 2018 d'Ocumension un paiement initial de 3 millions d'euros et recevra un paiement supplémentaire de 2,5 millions d'euros lorsque la Société initiera une étude clinique de phase 3 pour le NCX 470 en dehors du territoire objet de l'accord. La Société pourrait également recevoir dans le futur des paiements d'étapes potentiels supplémentaires d'un montant pouvant atteindre d'une part, 14,5 millions d'euros liés à l'avancement du développement de NCX 470 jusqu'à l'approbation réglementaire et, d'autre part, des paiements d'un montant pouvant atteindre 16,25 millions d'euros répartis sur trois étapes commerciales distinctes lorsque les ventes potentielles atteindront 200 millions d'euros sur le territoire précité, ainsi que des redevances échelonnées de 6% à 12% sur les ventes.

En mars 2020, Nicox a signé un amendement de l'accord sur le NCX 470 avec Ocumension. En vertu de cet amendement, Ocumension a payé à Nicox €15 millions en remplacement de l'intégralité des paiements d'étape du contrat initial (dont €14 millions sont remboursables sous certaines conditions). Ocumension a également acquis des droits exclusifs supplémentaires pour le NCX 470 pour la Corée et l'Asie du Sud-Est et paiera 50% des coûts de la deuxième étude clinique de phase 3 dans le glaucome (l'étude Denali) pour le NCX 470. Les deux sociétés mèneront conjointement cette étude aux Etats-Unis et en Chine. Aucun futur paiement d'étape pour le NCX 470 ne sera dû par Ocumension à Nicox. Dans le cas peu probable où l'étude conjointe ne serait pas menée à son terme, des remboursements partiels pourraient être effectués et, dans certaines situations, les paiements d'étape de l'accord initial seraient à nouveau applicables. Les redevances échelonnées de 6% à 12% de l'accord original restent inchangées et s'appliqueront aux ventes dans les territoires initiaux et supplémentaires.

La Société a considéré qu'il n'y avait pas de nouvelles obligations de performance dans le cadre de la signature de cet amendement et que 1 million d'euros pouvait être reconnu immédiatement en chiffre d'affaires. Les 14 millions d'euros résiduels (reconnus initialement en produits constatées d'avance) ne sont comptabilisés en chiffre d'affaires que dans la seule mesure où il devient hautement probable que la levée ultérieure de l'incertitude relative à la contrepartie variable et aux potentielles clauses de remboursement ne donneront pas lieu à un ajustement à la baisse important du montant cumulatif du chiffre d'affaires comptabilisé. Sur les 14 millions d'euros, reconnus initialement en produits constatés d'avance, les produits résiduels s'élèvent au 31 décembre 2022 à 1.5 millions d'euros et seront reconnus lorsqu'il deviendra hautement probable que la levée ultérieure de l'incertitude relative aux potentielles clauses de remboursement ne donne pas lieu à un ajustement à la baisse important du montant cumulatif du chiffre d'affaires comptabilisé.

Aucun chiffre d'affaires relatif à ce contrat n'a été reconnu en 2022 contre 3 millions d'euros sur l'ensemble de l'exercice 2021.

2.18.2.2 Bausch & Lomb

En mars 2010, la Société a signé un accord de licence avec Bausch + Lomb (société du groupe Valeant), leader de la santé oculaire, lui allouant les droits exclusifs mondiaux de développement et de commercialisation de Latanaprostene Bunod (solution ophtalmique de latanoprostène bunod à 0,024 %). Selon les termes de l'accord, Bausch + Lomb a versé un paiement initial de licence de $ 10 millions à la Société à la signature de l'accord, suivi d'un paiement d'étape additionnel de $ 10 millions en avril 2012 suite à la décision de poursuivre le développement de Latanaprostene Bunod après la finalisation de l'étude de phase 2b achevée fin 2011. La Société a reçu en 2017 un paiement d'étape de $17.5 millions suite à l'enregistrement de VYZULTA par la FDA le 2 novembre 2017.

La Société pourrait également recevoir dans le futur, des paiements potentiels supplémentaires pouvant atteindre un total maximum de $ 165 millions, conditionnés à la réalisation d'étapes réglementaires et commerciales, résultant en des paiements d'étapes nets pour la Société pouvant atteindre un total maximum de $ 150 millions après déduction des paiements dus à Pfizer dans le cadre de l'accord conclu en 2009. La Société devrait également recevoir d'éventuelles redevances nettes sur les ventes pouvant aller de 6 à 12 % après déduction des paiements dus à Pfizer.

Cet accord restera en vigueur jusqu'à l'expiration des obligations de paiement de redevances de Bausch + Lomb, à moins d'une résiliation anticipée par la Société ou Bausch + Lomb, conformément à la clause de résiliation anticipée prévue au contrat. La Société pourrait résilier cet accord pays par pays si Bausch + Lomb ne met pas en œuvre tous les efforts commerciaux raisonnables pour développer et commercialiser les produits sous licence dans le cadre de cet accord. Il pourrait également mettre fin à la totalité de cet accord si Bausch + Lomb conteste ou incite un tiers à contester la validité ou la propriété de ses brevets sous licence ou encore omet ou se trouve dans l'incapacité de remplir ses obligations de paiement dans le cadre de cet accord. En cas de résiliation, les licences que la Société a octroyées à Bausch + Lomb seraient résiliées et toute sous-licence octroyée par Bausch + Lomb serait soit attribuée à la Société soit résiliée.

2.18.2.3 Pfizer

En août 2009, la Société a conclu un contrat avec Pfizer mettant fin à leurs précédents accords de collaboration d'août 2004 et de mars 2006. Selon les termes de ce contrat, la Société a recouvré l'ensemble des droits de développement et de commercialisation du Latanoprostène Bunod (désormais connu sous le nom de marque VYZULTA) notamment le droit de sous-licencier, ainsi que la totalité des données et des informations de développement. Ce médicament est actuellement licencié à Bausch + Lomb (voir ci-dessus) et commercialisé depuis décembre 2017. Par ailleurs, la Société peut également accéder à certaines informations de développement du Xalatan (latanoprost) appartenant à Pfizer, notamment les dossiers réglementaires du Xalatan. En contrepartie, la Société s'est engagée à verser à Pfizer deux paiements d'étape de $15 millions chacun. Le premier paiement, qui était lié à l'approbation aux États-Unis de VYZULTA a été payé en décembre 2017. Le second est lié à la réalisation de niveaux de ventes prédéfinis. La Société est également redevable de redevances sur les ventes futures. La Société a également recouvré les droits d'un certain nombre de nouveaux composés donneurs d'oxyde nitrique, au stade de recherche, pour le traitement de la rétinopathie diabétique et du glaucome.

2.18.2.4 Fera Pharmaceutical

En novembre 2015, la Société a signé un contrat de licence exclusif avec Fera Pharmaceuticals, société pharmaceutique spécialisée à capitaux privés, pour le développement et la commercialisation du naproxcinod aux Etats-Unis. L'accord prévoit que Fera se concentrera dans un premier temps sur le traitement des signes et symptômes de l'arthrose, puis consultera la FDA américaine (*Food and Drug Administration*) au sujet des travaux cliniques supplémentaires requis avant de soumettre un dossier de *New Drug Application* (NDA) pour la naproxcinod. Fera Pharmaceuticals prendra en charge l'ensemble des activités et des coûts de développement clinique, de fabrication et de commercialisation.

Selon les termes du contrat, la Société pourrait toucher jusqu'à 40 millions de dollars sous formes de paiements liés à des étapes commerciales, plus 7% de redevances sur les futures ventes du naproxcinod aux Etats-Unis.

A noter que Fera Pharmaceuticals pourrait recevoir des redevances d'un montant non divulgué dans le cas où le naproxcinod serait approuvé et commercialisé en utilisant des données générées par Fera Pharmaceuticals, quels que soient l'indication thérapeutique et le territoire (hors Etats-Unis).

Au cours du second trimestre 2020, Nicox a été informé par son partenaire Fera que le dossier de désignation de médicament orphelin (Orphan Drug Designation, ODD) pour le naproxcinod dans la drépanocytose auprès de la FDA américaine a été refusé et qu'il réfléchit actuellement aux réponses qui pourraient être apportées à la lettre de la FDA. Fera examine également d'autres indications pour le développement du naproxcinod dont un potentiel traitement adjuvant de la COVID-19. Nicox et Fera ont amendé l'accord existant pour y inclure l'indication de la COVID-19 et Nicox a octroyé à Fera 10 000 bons de souscription d'actions correspondant à 10 000 actions Nicox.

En mars 2022, Nicox et Fera Pharmaceuticals ont annoncé que la *Food and Drug Administration* (FDA) américaine a accordé la désignation de médicament orphelin (Orphan Drug Designation) au naproxcinod dans le traitement de la drépanocytose, maladie qui touche environ 100 000 américains. Le naproxcinod est un naproxène donneur d'oxyde nitrique (NO) combinant l'activité inhibitrice de la cyclooxygénase (COX) du

naproxène avec celle de l'oxyde nitrique développé par Nicox et licencié exclusivement à Fera aux États-Unis. Nicox a testé le naproxcinod auprès de plus de 2 700 patients souffrant d'arthrose, ce qui a généré un ensemble important de données sur la sécurité clinique disponibles pour soutenir le développement du naproxcinod par Fera et, ultérieurement, une demande d'autorisation de mise sur le marché pour la drépanocytose

2.18.2.5 Passifs éventuels

En dehors des litiges liés aux activités courantes de la Société, et dont il est permis de penser qu'ils sont d'ores et déjà convenablement provisionnés ou qu'il est peu probable qu'ils engendrent un coût significatif pour la Société, les éléments suivants doivent être signalés.

- **Engagements envers les salariés et mandataires sociaux**

Les membres du comité de direction bénéficient d'une indemnité contractuelle de licenciement d'un montant compris entre six mois et deux ans de salaires en cas de changement de contrôle entraînant la rupture du contrat de travail dans les deux années qui suivent ce changement de contrôle majoritaire de la Société. Le calcul de l'indemnité est basé sur les salaires perçus par les bénéficiaires sur les douze derniers mois précédents la rupture du contrat de travail. Si la rupture du contrat de travail de l'ensemble des bénéficiaires intervenait au 31 décembre 2022, le montant de l'indemnité à verser dans le contexte des dispositions ci-dessus décrites s'élèveraient à 1 792 877€ .

En cas de rupture du contrat de travail à l'initiative du Groupe, les membres du comité de direction, recevraient également une indemnité contractuelle de licenciement comprise entre trois mois et dix-huit mois de salaires sur la base des salaires perçus les douze mois précédant la rupture du contrat de travail. La rupture pour faute grave ou lourde n'ouvre pas droit aux dispositions ci-dessus décrites. Par ailleurs le versement de l'indemnité au Directeur General est conditionné à la réalisation d'objectifs non divulgués. Si la rupture du contrat de travail de l'ensemble des bénéficiaires intervenait au 31 décembre 2022, le montant de l'indemnité à verser dans le contexte des dispositions ci-dessus décrites s'élèveraient à 1 554 316 €

En raison du caractère conditionnel des engagements ci-dessus décrits, le Groupe n'a pas comptabilisé de provision au titre de ces engagements au 31 décembre 2022 pour les personnes concernées.

- **Litige avec l'administration fiscale voir note 2.22**

- **Litige avec Teva Pharmaceutical**

Teva Pharmaceutical Industries Ltd a formé opposition à l'encontre du brevet européen couvrant le latanoprostene bunod devant l'Office Européen des Brevets le 23 novembre 2016 et a sollicité la révocation du brevet dans sa totalité en alléguant son défaut de nouveauté et d'activité inventive. L'Office Européen des Brevets a rejeté cette opposition et a décidé de maintenir le brevet tel que délivré. Teva Pharmaceuticals a interjeté appel de cette décision de l'OEB le 12 septembre 2018. Teva a retiré l'appel. Le 7 juillet 2022, la chambre de recours de l'OEB a clos la procédure de recours. La décision de l'OEB est devenue définitive et le brevet est maintenu tel que délivré.

- **Litige avec la société Gland Pharma**

Dans le cadre de la soumission d'une demande ANDA (Abbreviated New Drug Application) auprès de la FDA pour l'approbation d'une version générique de VYZULTA (latanoprostène bunod), la société Gland Pharma, société indienne spécialisée dans les médicaments génériques, soutient, conformément à une pratique usuelle, que les brevets couvrant VYZULTA ne sont pas valides. Le 30 juin 2022, Bausch + Lomb et Nicox ont conjointement déposé une plainte à l'encontre de Gland Pharma dans le New Jersey contestant cette allégation (les frais de cette procédure étant intégralement à la charge de Bausch + Lomb). Cette procédure judiciaire a pour effet de mettre en sommeil l'examen règlementaire de l'ANDA par la FDA pendant 30 mois. Conformément aux termes de l'accord de licence, Bausch + Lomb paiera l'ensemble des frais liés à cette procédure, Nicox de son côté prêtera assistance à Bausch + Lomb pour

fournir les documents et informations nécessaires. Il est estimé que la procédure judiciaire pourrait durer 3 ou 4 années. Si un ou plusieurs brevets devaient être invalidés (échéance de 3 ou 4 ans), ce que la Société estime peu probable, la Société ne recevrait plus de revenus de la part de Bausch + Lomb, étant précisé que les revenus impactés seront ceux générés aux Etats-Unis.

- **Litige avec l'Urssaf**

La Société a contesté l'assujettissement aux cotisations de sécurité sociale des rémunérations de l'activité des administrateurs versés à deux administrateurs mandataires sociaux non-salariés qui sont résidents fiscaux aux Etats-Unis. Par jugement du 24 janvier 2020, le Tribunal Judiciaire de Nice a fait droit aux demandes de la Société. L'URSSAF a interjeté appel de ce jugement pour demander son infirmation, la confirmation du redressement et, en conséquence, la condamnation de la Société à verser 95 054 euros à titre principal et 2 000 euros au titre de l'article 700 du Code de Procédure Civile. L'affaire avait été radiée du rôle en l'absence de diligences de la part de l'URSSAF. À la suite de nouvelles diligences, l'affaire a été réinscrite. L'audience de plaidoirie suite à la réinscription de l'affaire s'est tenue le 1 er décembre 2022 et le jugement a été mis en délibéré jusqu'au 2 févier 2023 (cf note 2.26 événements postérieurs à la clôture).

- **Option de vente des BSA émise au titre du placement privé réalisé en novembre 2022**

Le Société a réalisé en novembre 2022 une augmentation de capital sans droit préférentiel de souscription, par émission de 6 849 316 actions ordinaires nouvelles, chacune assortie d'un bon de souscription permettant de souscrire 6 849 316 nouvelles actions ordinaires supplémentaires pendant une période de cinq années suivant l'attribution des bons de souscription d'action (BSA). La souscription était réservée à une ou plusieurs sociétés ou fonds gestionnaires d'épargne collective de droit français ou de droit étranger ou personnes physiques investissant habituellement dans le secteur pharmaceutique/biotechnologique. Un seul investisseur (Armistice) a participé à cette levée de fonds. Ces BSA sont librement cessibles.

Le Conseil d'administration a fixé le prix d'exercice des BSA à 1,70 euros le 21 novembre 2022. Dans l'hypothèse où la Société ferait l'objet, durant la période où les BSA issus de la levée de fonds sont en circulation, d'une opération de fusion par absorption, d'une fusion par création d'une nouvelle société, d'une scission ou d'un changement de contrôle au sens de l'article L. 233-3 I du Code de commerce dont la rémunération consisterait en la remise de titres dont la parité d'échange ferait ressortir une valeur par action inférieure au prix d'exercice des BSA, Armistice aura la possibilité de demander à la Société (après la réalisation définitive de l'opération) de racheter ses BSA à un prix déterminé selon une formule Black Scholes. Le montant hypothétique de rachat au 31/12/2022 a été évalué à 4 181 994€. Les hypothèses à utiliser dans le calcul de Black Scholes, y compris un niveau minimum de volatilité, ont été définies dans le contrat des BSA. En cas de cession des BSA à un autre porteur, le droit de demander le rachat des BSA ne lui serait pas transféré.

2.19 Rémunération des dirigeants et des mandataires sociaux

Le montant global des rémunérations comptabilisées au 31 Décembre 2022 pour les Administrateurs (comme en 2021) est récapitulé dans le tableau ci-dessous :

	2022	**2021**
	(en milliers d'Euros)	
Avantages à court terme	1 487	773
Avantages postérieurs à l'emploi	70	93
Total	**1 557**	**866**

Au 31 décembre 2022, les options de souscription d'actions, les bons de souscription d'actions et les actions gratuites en circulation attribués à des mandataires sociaux, se répartissent comme suit :

Nature des instruments de capitaux propres	**Prix d'exercice ou de souscription par bon en €**	**Nombre de BSA, d'options ou d'actions gratuites**	**Nombre d'actions à émettre**	**Date d'expiration**
Actions gratuites		525 000	525 000	
Bons de souscription d'actions	8.88	120 000	120 000	24/05/23
Options de souscription d'actions	6.05	60 000	60 000	12/02/27
Option de souscription d'actions	4.79	190 000	190 000	27/01/28
Option de souscription d'actions	3.52	180 000	180 000	14/01/29
Option de souscription d'actions	2.37	285 000	285 000	15/02/30
Option de souscription d'actions	1.80	1 139 998	1 139 998	18/07/30

2.20 Honoraires des Commissaires aux comptes et des membres de leur réseau

L'Emetteur s'entend comme étant la société mère, Nicox S.A.

	Ernst & Young Audit				Approbans			
	Montant (HT)		en %		Montant (HT)		en %	
	2021	2022	2021	2022	2021	2022	2021	2022
Audit								
Commissariat aux comptes, certifications, examen des comptes individuels et consolidés								
Emetteur	161 000	154 000	69.73%	75,42%	26 000	28 000	57.78%	73.78%
Filiales intégrées	12 000	12 000	5.20%	5.88%				
Autres diligences et prestations directement liées à la mission du commissaire aux comptes								
Emetteur (Requis par la législation nationale)	57 900	38 202	25.08%	18,71%	19 000	10 000	42.22%	26.32%
Sous-total	230 900	204 202	100.00%	100.00%	45 000	38 000	100.00%	100,00%
Autres prestations rendues par les réseaux								
Fiscal			0.00%	0.00%				
Autres (à préciser si>10% des honoraires d'audit)								
Sous-total			0.00%	0.00%				
TOTAL	**230 900**	**204 202**			**45 000**	**38 000**		

2.21 Effectif

A la clôture de l'exercice, la Société emploie 11 personnes.

Sur les 11 personnes salariées de la Société :

- 11 sont en CDI
- 8 travaillent dans les services Administration & Corporate et 3 dans les autres services

2.22 Impôts et situation fiscale latente

A la clôture de l'exercice la situation fiscale de la Société s'analyse comme suit :

- Produit de CIR afférent à l'année 2022 : 504 372€
- Déficits ordinaires indéfiniment reportables : 490 857 604€

En février 2019, la Société a été notifié d'un contrôle fiscal portant sur les exercices 2016, 2017 et entendu à 2018 sur certains éléments fiscaux. Le contrôle s'est achevé en septembre 2020 par une notification de redressement portant sur 49,6 millions d'euros de déficits reportables sur un total de 484,6 millions d'euros disponibles au 31 décembre 2020 ainsi que sur un montant de 0,7 million d'euros de retenue à la source. La Société a contesté fermement le bienfondé de ces redressements et en a informé l'administration par courrier le 10 novembre 2020.

En mars 2021 l'administration a abandonné la remise en cause d'une partie du déficit reportable pour 24,8 millions d'euros. En 2021, la Société était engagée dans une procédure de recours hiérarchique avec l'administration fiscale qui s'est soldé par le maintien par l'administration des deux redressements résiduels.

Au cours du premier semestre 2022, la somme de 0,7 million d'euros de retenue à la source a été mise en recouvrement et la Société s'est acquittée de cette somme. La Société a effectué une réclamation au sujet de la mise en recouvrement de cette somme, celle-ci a été rejetée en date du 5 septembre 2022. La Société a saisi le Tribunal administratif d'une demande de dégrèvement du supplément d'imposition au titre de la retenue à la source, pénalités comprises le 4 novembre 2022. Le Tribunal administratif a accusé réception de la saisine le 8 novembre 2022. La Société n'a pas enregistré de provisions concernant ce litige.

Concernant le second point en redressement, c'est-à-dire la contestation des déficits reportables découlant des activités commerciales de la Société avant 2016, la Société a renoncé à saisir le tribunal administratif en la matière et a corrigé ses déficits reportables de 24,8 millions d'euros en les minorant sur la liasse fiscale de cet exercice. Après imputation de cette déduction, les déficits reportables de la Société s'élèvent à 490 857 604€ au 31 décembre 2022.

2.23 Filiales et participation

Filiales et participations détenues au 31 décembre 2022

A la clôture de l'exercice Nicox SA détient des participations dans 2 sociétés :

- Nicox Research Institute, société à responsabilité limitée de droit italien créée en octobre 1999 et détenue à 100% par Nicox S.A.
- Nicox Ophtalmics Inc, société américaine acquise le 22 octobre 2014 détenue à 100% par Nicox SA

Tableau des filiales et participations :

En Euros	**Nicox Research Institute**	**Nicox Ophthalmics Inc.**
Capital Social	100 000	9
Capitaux propres autres que le capital (avant affectation du résultat)	**(3 728 331)**	**33 023 023**
Quote-part de capital détenue	100%	100%
Valeur comptable des titres détenus brute	**1 009 760**	**54 621 792**
Prêts et avances consentis par la Société et non encore remboursés	0	**36 134 303**
Valeur comptable nette des prêts et avances	0	**36 134 303**
Cautions et avals donnés par la Société		**-**
Chiffre d'affaires hors taxes du dernier exercice clos au 31 décembre 2022	**1 754 420**	**1 631 751**
Résultat (bénéfice ou perte du dernier exercice clos au 31 décembre 2022)	**99 176**	**(3 972 145)**
Dividendes encaissés par la Société au cours de l'exercice	-	-

2.24 Relations avec les parties liées

Conformément à l'article R.225-30 du Code de commerce, nous vous informons qu'il n'existe pas de convention soumise à l'article L.225-38 et suivants du Code de commerce conclue antérieurement au 1er janvier 2022 qui se soit poursuivie au cours de l'exercice clos le 31 décembre 2022.

Nous vous rappelons qu'aucun accord relevant des articles L.225-38 et suivants du Code de commerce n'a été conclu au cours de l'exercice clos le 31 décembre 2022.

2.25 Comptes consolidés

Des comptes consolidés ont été préparés par Nicox S.A. au 31 décembre 2022. Les comptes consolidés du Groupe comprennent en intégration globale les comptes de Nicox S.A et de ses filiales détenues à 100%, Nicox Research Institute et Nicox Ophthalmics Inc. Les soldes et opérations réciproques entre les sociétés du Groupe ont été éliminés. Les comptes de toutes les filiales sont clôturés au 31 décembre.

2.26 Conflit Ukraine/Russie

Il n'a pas été relevé d'impacts directs à venir sur la situation financière de la Société à la suite du conflit Russie / Ukraine, déclaré au cours du mois de février 2022. En effet, à la date de ce présent document, la Société ne possède aucun client dans ces territoires et ne projette pas d'y développer une activité significative à court ou moyen terme.

La Société n'a également aucune exposition directe en termes de recherche et développement. Néanmoins, bien que ce conflit n'ait pas d'impacts significatifs sur la performance de la Société, ce dernier ne peut, à ce stade, présager des conséquences macroéconomiques de cette situation géopolitique et de son évolution sur sa performance future.

2.27 Tableau des résultats des 5 derniers exercices

	31-12-2022	31-12-2021	31-12-2020	31-12-2019	31-12-2018
CAPITAL EN FIN D'EXERCICE					
Capital social	50 100 448	43 138 185	37 030 335	33 230 570	29 718 920
-Nombre d'actions ordinaires	50 100 448	43 138 185	37 030 335	33 230 570	29 718 920
-Nombre d'action à créer par droit de souscription	17 459 314	7 925 498	1 394 800	1 175 620	1 263 740
OPERATIONS & RESULTATS					
Chiffre d'affaires hors taxes	5 453 301	6 719 332	14 588 755	4 051 734	5 299 962
Résultat avant impôts, participation, dotations aux amortissements & provisions	-19 593 315	-13 155 725	-18 077 590	-14 478 826	-10 788 757
Impôt sur les bénéfices (crédit d'impôt recherche)	504 372	716 324	735 673	864 066	840 078
Participation des salariés	0	0	0	0	0
Dotations aux amortissements & provisions	12 196 037	37 898 091	-5 253 701	7 415 812	204 359
Résultat net	-31 284 980	-50 337 492	-12 088 165	-21 030 573	-10 152 856
Résultat distribué					
RESULTAT PAR ACTION					
Résultat après impôt, participation, mais avant dotations aux amortissements & provisions	-0.39	-0.30	-0,49	-0.67	-0.36
Résultat net	-0.62	-1.17	-0,33	-0.63	-0.34
Résultat net dilué	-0.62	-1.17	-0,33	-0.63	-0.34
Dividende attribué					
PERSONNEL					
Effectif moyen	12	15	15	17	16
Masse salariale	3 052 983	2 091 591	2 219 207	2 252 066	2 189 774
Somme versée au titre des avantages sociaux [sécurité sociale, œuvres sociales, etc.]	1 176 890	952 285	1 170 468	1 018 879	1 131 999

2.28 Objectifs et politiques de gestion des risques financiers

Les besoins de financement de la Société ont été, à ce jour, principalement assurés par des levées de fonds sur le marché financier qui ont généré des augmentations de capital par émission de nouvelles actions, des revenus issus d'accord de licence avec des partenaires et des remboursements de créances de crédit d'impôt recherche.

L'objectif de la Société en matière de gestion du capital est de gérer efficacement ses liquidités de façon à assurer le financement de ses activités de recherche et développement.

2.28.1 Risque de change

La Société communique son information financière en euros. La majorité des dépenses encourues par la Société sont libellées en euros. Certaines dépenses et certains revenus tirés des ententes conclues avec les partenaires pharmaceutiques de la Société sont cependant libellés en dollars américains. Au cours de l'exercice 2022, environ 58.43% des dépenses opérationnelles ont été réalisées en dollars américains. (60.20% en 2021).

Les paiements des redevances ainsi que les paiements d'étapes libellés en dollars attendus par la Société notamment au travers du contrat de licence exclusif mondial accordé à Bausch + Lomb pour VYZULTA ne sont pas suffisamment significatifs pour que les fluctuations du cours de l'euro par rapport au dollar américain aient un impact matériel sur le résultat opérationnel de la Société.

La Société détient également des comptes bancaires libellés en dollars américains, qui sont convertis en euros au taux de change en vigueur à la date de clôture. Le montant de trésorerie concernée s'élève à 7 349 272€ au 31 décembre 2022 soit 27.1 % de la trésorerie disponible et pourrait être impacté par une variation significativement importante du cours €/$. Ce risque est toutefois pondéré par le fait que cette trésorerie est exclusivement destinée à couvrir les dépenses libellées en $ qui résultent des activités de recherche et développement réalisées aux Etats-Unis à moyen terme.

La Société n'utilise pas de produits dérivés et n'a pas mis en place de procédures internes spécifiques pour mitiger le risque de change.

La Société ne détient pas d'actifs financiers ni de dette bancaire libellés en devise étrangère.

2.28.2 Risque de taux d'intérêt

La Société n'est pas exposée aux fluctuations des taux d'intérêts car les équivalents de trésorerie sont exclusivement composés de comptes à terme à taux fixes.

2.28.3 Risque de marché

Au 31 décembre 2022, la Société ne dispose pas d'instruments financiers et n'est donc pas exposé au risque de marché.

2.28.4 Risque de liquidité

La Société ne détient pas de prêt auprès d'établissements de crédit qui pourrait se prévaloir d'une clause de remboursement anticipé.

Dans l'ensemble, les activités sont déficitaires et pourraient le rester à court terme. Au 31 décembre 2022, la Société détenait €27.1 millions en trésorerie et équivalents de trésorerie (€41.2 millions au 31 décembre 2021).

Dans le cadre de la restructuration de son prêt avec Kreos Capital (cf note 2.10) 3,3 millions d'euros du capital restant ont été émis sous forme d'obligations convertibles. L'échéance est le 1er janvier 2026 avec le même taux d'intérêt que le prêt initial soit de 9,25 % par an, payable en espèces. Le prêt convertible est garanti par les mêmes garanties déjà en place pour le prêt à terme. Cette partie de la dette peut être convertie en actions au gré de Kreos à tout moment (après une période initiale de 60 jours) jusqu'à l'échéance du 1er janvier 2026. Le prix de conversion est de 3,67 €. Si l'évolution du cours de l'action Nicox ne permettait pas de convertir les obligations avant l'échéance du 1 er juillet 2026 le montant total du Prêt Convertible restant serait dû en un seul versement à ce moment-là.

La Société détient un contrat de liquidité qui est adossé à un contrat d'animation du titre. L'exposition au risque est limitée à un investissement maximum de 1 million d'euros. La moins-value latente au titre de ce contrat au 31 décembre 2022 s'élevait à 655 000 €.

Grace à la restructuration de son accord de financement obligataire avec Kreos Capital en décembre 2021 suivie de l'exercice en novembre 2022 de l'option d'extension de six mois supplémentaires de la période de paiement des intérêts sans remboursement du capital ainsi que la réalisation également en novembre 2022 d'une augmentation de capital de 10 millions d'euros brut réservée à des investisseurs institutionnels spécialisés, la Société a étendu son horizon de trésorerie jusqu'au deuxième trimestre 2024.

La société est à la recherche continue de nouvelles sources de financement permettant d'assurer la continuité de ses activités de recherche et développement.

2.28.5 Risque de crédit

Il n'existe *a priori* pas de risque de recouvrement de la créance liée au Crédit d'Impôt Recherche, étant donné qu'il s'agit d'une créance de l'Etat français.

Concernant les autres actifs financiers de la Société, à savoir la trésorerie, les équivalents de trésorerie, l'exposition au risque de crédit est conditionnelle à un potentiel défaut de paiement des tiers concernés.

A ce jour, les équivalents de trésorerie sont composés à 100% de comptes à terme.

2.29 Évènements postérieurs à la clôture

L'assemblée générale du 28 février 2023 a approuvé le transfert de la cotation des titres émis par la Société du Compartiment C du marché réglementé Euronext Paris vers le système multilatéral de négociation Euronext Growth Paris et ont donné au Conseil d'administration tous les pouvoirs pour la réalisation de ce transfert. Le transfert vers Euronext Growth Paris, qui est soumis à l'accord de l'entreprise de marché Euronext Paris, a été approuvé par Euronext Listing Board le 24 avril 2023. Cette opération vise à permettre à la Société de voir ses titres admis aux négociations sur un marché plus en rapport avec sa taille et sa capitalisation boursière.

En date du 2 Février 2023, la Cour d'Appel a confirmé le jugement en première instance dans le litige qui opposait le Groupe à l'Urssaf relatif aux cotisations de sécurité sociale des rémunérations versées, au titre de leur mandat, à deux administrateurs mandataires sociaux non-salariés qui sont résidents fiscaux aux Etats-Unis.

PART 5 - STATUTORY AUDITORS' REPORT ON THE CONSOLIDATED FINANCIAL STATEMENTS

1. Statutory Auditors' report on the Consolidated Financial Statements

Approbans Audit | Ernst & Young Audit

Nicox S.A.
Year ended December 31, 2022

Statutory auditors' report on the consolidated financial statements

Approbans Audit
22, boulevard Charles Moretti
La Palmeraie du Canet
13014 Marseille
S.A.R.L. with share capital of € 100 000
Companies Register (RCS) No.°5 525 098 786 Marseille

Statutory Auditors
Member of the Regional Association of Chartered Accountants
of Aix-Bastia

Ernst & Young Audit
Tour First
TSA 14444
92037 Paris-La Défense cedex
S.A.S with variable capital
Companies Register (RCS) No.°344 366 315. Nanterre

Statutory Auditors
Member of the Regional Association
of Chartered Accountants of Versailles and the Central
Region

This is an unsigned free translation into English of the Statutory Auditors' report issued in French and is provided solely for the convenience of English speaking readers. The Statutory Auditors' report includes information specifically required by French law in such reports, whether qualified or not. This information is presented below the opinion on the financial statements and includes an explanatory paragraph discussing the auditors' assessments of certain significant accounting and auditing matters. These assessments were considered for the purpose of issuing an audit opinion on the financial statements taken as a whole and not to provide separate assurance on individual account balances, transactions, or disclosures. This report also includes information relating to the specific verification of information given in the Group management report and in the documents addressed to shareholders. This report should be read in conjunction with, and construed in accordance with, French law and professional auditing standards applicable in France.

Nicox S.A.

Year ended December 31, 2022

Statutory auditors' report on the consolidated financial statements

To Nicox SA's General Meeting:

Opinion

In accordance with the terms of our engagement as auditors entrusted to us by ***your General Meetings, we have audited the accompanying consolidated financial statements of Nicox S.A. for the year ended December 31, 2022.

In our opinion, the consolidated financial statements give a true and fair view of the results of the operations of the Group for the year then ended and of its financial position and its assets and liabilities as at December 31, ***2021 in accordance with International Financial Reporting Standards as adopted by the European Union.***

The audit opinion expressed above is consistent with our report to the Audit Committee.

Basis for opinion

Audit framework

We conducted our audit in accordance with professional standards applicable in France. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Our responsibilities under those standards are further described in the "Statutory Auditors' Responsibilities for the audit of the annual financial statements" section of our report.

Independence

We conducted our audit engagement in compliance with the independence rules provided for in the French Commercial Code (*Code de commerce*) and the French Code of Ethics (*Code de Déontologie*) for Statutory Auditors, for the period from 1 January 2022 to the date of our report, and, in particular, we did not provide any non-audit services prohibited by Article 5(1) of Regulation (EU) No. 537/2014.

Justification of assessments - Key audit matters

In accordance with the requirements of articles L. 823-9 and R. 823-7 of the French commercial code relating to the justification of our assessments, we bring your attention to the key audit matters relating to risks of material misstatement that, in our professional judgment, were of most significance in the audit of the consolidated financial statements of the current period, as well as our responses to those risks.

These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon. We do not provide a separate opinion on specific items of the consolidated financial statements.

Recoverable value of goodwill and other intangible assets

Identified risk	Our response
As of December 31, 2022, the net book value of the goodwill and other intangible assets of your group amounted to €27.2 million and €31.7 million respectively, in relation to total assets of €93.2 million. It should be noted that in February 2022, your group announced that the development of NCX 4251 would focus on dry eye disease rather than the indication for blepharitisas as initially planned. Your group completely revised its development plan for NCX 4251 resulting in an impairment of this asset in December 2021 in the amount of US$17.8 million. On June 30, 2022, your group decided to seek a partner to pursue the product's development outside China and as a consequence recognized an additional impairment charge of US$11.5 million at December 31 2022. The net book value of NCX 4251 after impairment is now US$3.7 million, or €3.5 million. Goodwill and indefinite lived*** intangible assets are tested for impairment at least once a year during the last quarter, and whenever there is an indication that the asset may be impaired. Tests are performed for other amortized intangible assets whenever there is an indication that the asset may be impaired. They are based on the recoverable value defined as the higher of its net selling price and value in use where the latter is defined as the present value of estimated future operating cash flows according to medium term strategic plans, and extrapolated for the subsequent periods. We considered that the determination of the recoverable amount for goodwill and other intangible assets constituted a key audit point in light of their importance in the consolidated financial statements and because the determination of value in use is based on assumptions, estimates or assessments, as indicated in notes 3.7, 4.6 and 9 to the consolidated financial statements.	Our procedures consisted primarily in: ►examining the main assumptions used and notably the cash flow forecasts and comparing them with the advancement of projects and the results of the clinical studies obtained from these projects. We also compared this information with our knowledge of the environment and, where possible, with third-party data; ►examining market projections with respect to available and comparable data and performing sensitivity tests on the impairment tests conducted by management; ►obtaining the input of the valuation specialists on our audit team to review the methodology adopted by management, the mathematical model and the discount rates; ►examining the consistency of the accounting principles adopted by management; ► assessing the appropriateness of the disclosures in the notes to the consolidated financial statements.

Specific procedures

As required by French law and regulations, we also performed the specific verifications, in accordance with professional standards applicable in France, of the information provided on the group presented in the Board of Directors' management report.

We have nothing to report with respect to the fair presentation of such information and its consistency with the consolidated financial statements.

Other verifications or disclosures required by legal and regulatory provisions

■ Appointment of the auditors

We were appointed as statutory auditors of Nicox S.A. by your general meeting of June 16, 2020 for APPROBANS AUDIT and of May 28, 1999 for ERNST & YOUNG Audit.

As at December 31, 2022, APPROBANS AUDIT was in the third year of its uninterrupted engagement and ERNST & YOUNG Audit in its twenty-fourth year

Responsibilities of management and those charged with governance for the consolidated financial statements

Management is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with International Financial Reporting Standards as adopted by the European Union, and for such internal control as management determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.***-***

In preparing the consolidated financial statements, Management is responsible for assessing the company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern, and using the going concern basis of accounting, unless it expects to liquidate the company or to cease operations.

The audit committee is responsible for monitoring the financial reporting process and the effectiveness of internal control and risk management systems and, where applicable, its internal audit, regarding the accounting and financial reporting procedures.

The consolidated financial statements have been approved by the Board of Directors

Statutory auditors' responsibilities for the audit of the consolidated financial statements

■ Objective and audit approach

Our role is to issue a report on the consolidated financial statements. Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with professional standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these annual*** financial statements.

As specified by article L. 823-10-1 of the French commercial code ("*code de commerce*"), the scope of our statutory audit does not include assurance on the future viability of the Company or the quality with which Company's management has conducted or will conduct the affairs of the entity.

As part of an audit conducted in accordance with professional standards applicable in France, the Statutory Auditors exercise professional judgment throughout the audit. They also:

- identify and assess the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion.***-*** The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of Internal Control;***-***
- obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal control;
- evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management in the consolidated financial statements;
- assess the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. Our conclusions are based on the audit evidence obtained up to the date of our audit report. However, future events or conditions may cause the Company to cease to continue as a going concern. If we conclude that a material uncertainty exists, we draw attention in our audit report to the related disclosures in the annual financial statements or, if such disclosures are not provided or inadequate, we issue a qualified opinion or no opinion at all;
- evaluate the overall presentation of the consolidated financial statements and assess whether these statements represent the underlying transactions and events in a manner that achieves fair presentation,
- obtain sufficient appropriate audit evidence regarding the financial information of the entities included in the consolidation scope to express an opinion on the consolidated financial statements. The Statutory Auditors are responsible for the management, supervision and performance of the audit of the consolidated financial statements and for the opinion expressed thereon.

Report to the Audit Committee

We submit a report to the audit committee which includes in particular a description of the scope of the audit and the audit program implemented, as well as significant audit findings. We also report any significant deficiencies in internal control that we have identified regarding the accounting and financial reporting procedures.

Our report to the Audit Committee includes information about the risks of material misstatement that, in our professional judgment, were of most significance in the audit of the consolidated financial statements of the current period and which are therefore the key audit matters. We describe these matters in the audit report.

We also provide the audit committee with the declaration referred to in article 6 of Regulation (EU) No. 537/2014, confirming our independence within the meaning of the rules applicable in France as defined in particular by Articles L. 822-10 to L. 822-14 of the French Commercial Code ("*code de commerce*") and in the French Code of Ethics for Statutory Auditors. Where appropriate, we discuss any risks to our independence and the related safeguard measures with the Audit Committee.

Marseille and Paris-La Défense, April 28, 2023

Statutory Auditors

French original signed by:

Approbans Audit	Ernst & Young Audit
Pierre Chauvet	Pierre Chassagne

2. Statutory Auditors' report on the Annual Financial Statements

APPROBANS AUDIT

ERNST & YOUNG Audit

Disclaimer: Statutory Auditors' report on the Annual Financial Statements is available in French only

Nicox S.A.

Exercice clos le 31 décembre 2022

Rapport des commissaires aux comptes sur les comptes annuels

Statutory Auditors' report on the Annual Financial Statements is available in French only

APPROBANS AUDIT
22, boulevard Charles Moretti
La Palmeraie du Canet
13014 Marseille
S.A.R.L. au capital de € 100 000
525 098 786 R.C.S. Marseille

Commissaire aux Comptes
Membre de la compagnie
régionale d'Aix-Bastia

ERNST & YOUNG Audit
Tour First
TSA 14444
92037 Paris-La Défense cedex
S.A.S. à capital variable
344 366 315 R.C.S. Nanterre

Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

Nicox S.A.

Exercice clos le 31 décembre 2022

Rapport des commissaires aux comptes sur les comptes annuels

A l'Assemblée Générale de la société Nicox S.A.,

Opinion

En exécution de la mission qui nous a été confiée par vos assemblées générales, nous avons effectué l'audit des comptes annuels de la société Nicox S.A. relatifs à l'exercice clos le 31 décembre 2022, tels qu'ils sont joints au présent rapport.

Nous certifions que les comptes annuels sont, au regard des règles et principes comptables français, réguliers et sincères et donnent une image fidèle du résultat des opérations de l'exercice écoulé ainsi que de la situation financière et du patrimoine de la société à la fin de cet exercice.

L'opinion formulée ci-dessus est cohérente avec le contenu de notre rapport au comité d'audit.

Fondement de l'opinion

Référentiel d'audit

Nous avons effectué notre audit selon les normes d'exercice professionnel applicables en France. Nous estimons que les éléments que nous avons collectés sont suffisants et appropriés pour fonder notre opinion.

Les responsabilités qui nous incombent en vertu de ces normes sont indiquées dans la partie « Responsabilités des commissaires aux comptes relatives à l'audit des comptes annuels » du présent rapport.

Indépendance

Nous avons réalisé notre mission d'audit dans le respect des règles d'indépendance prévues par le Code de commerce et par le Code de déontologie de la profession de commissaire aux comptes sur la période du 1er janvier 2022 à la date d'émission de notre rapport, et notamment nous n'avons pas fourni de services interdits par l'article 5, paragraphe 1, du règlement (UE) n° 537/2014.

Nous attestons de la sincérité et de la concordance avec les comptes annuels des informations relatives aux délais de paiement mentionnées à l'article D. 441-6 du Code de commerce.

- **Informations relatives au gouvernement d'entreprise**

Nous attestons de l'existence, dans la section du rapport de gestion du conseil d'administration consacrée au gouvernement d'entreprise, des informations requises par l'article L. 225-37-4 du Code de commerce.

- **Autres informations**

En application de la loi, nous nous sommes assurés que les diverses informations relatives à l'identité des détenteurs du capital ou des droits de vote vous ont été communiquées dans le rapport de gestion.

Autres vérifications ou informations prévues par les textes légaux et réglementaires

- **Désignation des commissaires aux comptes**

Nous avons été nommés commissaires aux comptes de la société Nicox S.A. par votre assemblée générale du 16 juin 2020 pour le cabinet APPROBANS AUDIT et du 28 mai 1999 pour le cabinet ERNST & YOUNG Audit.

Au 31 décembre 2022, le cabinet APPROBANS AUDIT était dans la troisième année de sa mission sans interruption et le cabinet ERNST & YOUNG Audit dans la vingt-quatrième année.

Responsabilités de la direction et des personnes constituant le gouvernement d'entreprise relatives aux comptes annuels

Il appartient à la direction d'établir des comptes annuels présentant une image fidèle conformément aux règles et principes comptables français ainsi que de mettre en place le contrôle interne qu'elle estime nécessaire à l'établissement de comptes annuels ne comportant pas d'anomalies significatives, que celles-ci proviennent de fraudes ou résultent d'erreurs.

Lors de l'établissement des comptes annuels, il incombe à la direction d'évaluer la capacité de la société à poursuivre son exploitation, de présenter dans ces comptes, le cas échéant, les informations nécessaires relatives à la continuité d'exploitation et d'appliquer la convention comptable de continuité d'exploitation, sauf s'il est prévu de liquider la société ou de cesser son activité.

Il incombe au comité d'audit de suivre le processus d'élaboration de l'information financière et de suivre l'efficacité des systèmes de contrôle interne et de gestion des risques, ainsi que le cas échéant de l'audit interne, en ce qui concerne les procédures relatives à l'élaboration et au traitement de l'information comptable et financière.

Les comptes annuels ont été arrêtés par le conseil d'administration.

Responsabilités des commissaires aux comptes relatives à l'audit des comptes annuels

Objectif et démarche d'audit

Il nous appartient d'établir un rapport sur les comptes annuels. Notre objectif est d'obtenir l'assurance raisonnable que les comptes annuels pris dans leur ensemble ne comportent pas d'anomalies significatives. L'assurance raisonnable correspond à un niveau élevé d'assurance, sans toutefois garantir qu'un audit réalisé conformément aux normes d'exercice professionnel permet de systématiquement détecter toute anomalie significative. Les anomalies peuvent provenir de fraudes ou résulter d'erreurs et sont considérées comme significatives lorsque l'on peut raisonnablement s'attendre à ce qu'elles puissent, prises individuellement ou en cumulé, influencer les décisions économiques que les utilisateurs des comptes prennent en se fondant sur ceux-ci.

Comme précisé par l'article L. 823-10-1 du Code de commerce, notre mission de certification des comptes ne consiste pas à garantir la viabilité ou la qualité de la gestion de votre société.

Dans le cadre d'un audit réalisé conformément aux normes d'exercice professionnel applicables en France, le commissaire aux comptes exerce son jugement professionnel tout au long de cet audit. En outre :

- il identifie et évalue les risques que les comptes annuels comportent des anomalies significatives, que celles-ci proviennent de fraudes ou résultent d'erreurs, définit et met en œuvre des procédures d'audit face à ces risques, et recueille des éléments qu'il estime suffisants et appropriés pour fonder son opinion. Le risque de non-détection d'une anomalie significative provenant d'une fraude est plus élevé que celui d'une anomalie significative résultant d'une erreur, car la fraude peut impliquer la collusion, la falsification, les omissions volontaires, les fausses déclarations ou le contournement du contrôle interne ;
- il prend connaissance du contrôle interne pertinent pour l'audit afin de définir des procédures d'audit appropriées en la circonstance, et non dans le but d'exprimer une opinion sur l'efficacité du contrôle interne ;
- il apprécie le caractère approprié des méthodes comptables retenues et le caractère raisonnable des estimations comptables faites par la direction, ainsi que les informations les concernant fournies dans les comptes annuels ;
- il apprécie le caractère approprié de l'application par la direction de la convention comptable de continuité d'exploitation et, selon les éléments collectés, l'existence ou non d'une incertitude significative liée à des événements ou à des circonstances susceptibles de mettre en cause la capacité de la société à poursuivre son exploitation. Cette appréciation s'appuie sur les éléments collectés jusqu'à la date de son rapport, étant toutefois rappelé que des circonstances ou événements ultérieurs pourraient mettre en cause la continuité d'exploitation. S'il conclut à l'existence d'une incertitude significative, il attire l'attention des lecteurs de son rapport sur les informations fournies dans les comptes annuels au sujet de cette incertitude ou, si ces informations ne sont pas fournies ou ne sont pas pertinentes, il formule une certification avec réserve ou un refus de certifier ;
- il apprécie la présentation d'ensemble des comptes annuels et évalue si les comptes annuels reflètent les opérations et événements sous-jacents de manière à en donner une image fidèle.

Rapport au comité d'audit

Nous remettons au comité d'audit un rapport qui présente notamment l'étendue des travaux d'audit et le programme de travail mis en œuvre, ainsi que les conclusions découlant de nos travaux. Nous portons également à sa connaissance, le cas échéant, les faiblesses significatives du contrôle interne que nous avons identifiées pour ce qui concerne les procédures relatives à l'élaboration et au traitement de l'information comptable et financière.

Parmi les éléments communiqués dans le rapport au comité d'audit figurent les risques d'anomalies significatives, que nous jugeons avoir été les plus importants pour l'audit des comptes annuels de l'exercice et qui constituent de ce fait les points clés de l'audit, qu'il nous appartient de décrire dans le présent rapport.

Nous fournissons également au comité d'audit la déclaration prévue par l'article 6 du règlement (UE) n° 537/2014 confirmant notre indépendance, au sens des règles applicables en France telles qu'elles sont fixées notamment par les articles L. 822-10 à L. 822-14 du Code de commerce et dans le Code de déontologie de la profession de commissaire aux comptes. Le cas échéant, nous nous entretenons avec le comité d'audit des risques pesant sur notre indépendance et des mesures de sauvegarde appliquées.

Marseille et Paris-La Défense, le 28 avril 2023

Les Commissaires aux Comptes

APPROBANS AUDIT	ERNST & YOUNG Audit
Pierre Chauvet	Pierre Chassagne