Press Release

Nicox Outlines Future Development and Partnering Plans for NCX 470 in Glaucoma

- **Outcome of the Mont Blanc Phase 3 trial suggests potential commercial opportunity of NCX 470 in the United States as a novel alternative treatment for intraocular pressure lowering**
- **Plans to generate clinical data aiming to demonstrate the potential retinal benefits of NCX 470 in order to add significant therapeutic value to the product profile in glaucoma**
- **Intention to harness the value of NCX 470 through the right commercial partnerships in the United States and Japan**

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Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced future development and partnering plans for NCX 470, a novel nitric oxide (NO)-donating bimatoprost eye drop, currently in Phase 3 development for the lowering of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

"*Our market research shows an unmet need in glaucoma treatment focused on lowering of intraocular pressure. Patients do not react to glaucoma medications in the same way, with up to 40% not achieving their target intraocular pressure on existing monotherapies, and therefore eye care professionals need multiple treatment options. Based on a dual mechanism of action, NCX 470 has been shown to be an effective agent for lowering intraocular pressure. Mont Blanc, the first of two Phase 3 trials for NCX 470, met the efficacy requirement for approval in the United States whilst demonstrating good tolerability in comparison to current products. The Mont Blanc trial demonstrated that NCX 470 reduced intraocular pressure by 8-9.7 mmHg, achieving its primary objective of demonstrating non-inferiority to latanoprost and we believe that NCX 470 can be successfully commercialized in key glaucoma markets including the United States, as well as China, where we have partnered with Ocumension Therapeutics. We are also planning to meet with the European Medicines Agency to discuss the regulatory requirements for the approval of NCX 470 in Europe,*" said **Andreas Segerros, Chief Executive Officer of Nicox**. "*In parallel, we plan to strengthen the profile of NCX 470 to maximize its therapeutic and commercial potential, by generating clinical data highlighting its potential retinal benefits, and we expect to support this with additional detailed analysis of the intraocular pressure data from the Mont Blanc trial together with planned nonclinical studies.*"

"*We are enthusiastic concerning the potential of NCX 470 in the Chinese market, based on the positive results from the Mont Blanc trial. 8 to 9.7 mmHg reduction in intraocular pressure sets the stage for the launch of this product as a new entrant in the Chinese glaucoma market. We look forward to continuing the collaboration with Nicox to bring NCX 470 to market,*" **said Liu Ye, Chief Executive Officer of Ocumension Therapeutics**.

Potential partnership opportunities for NCX 470

"*To complement our strong Chinese partnership, and maximize the potential future value of NCX 470, we are actively exploring commercial partnerships for NCX 470 in both the United States and Japanese markets,*" **said Gavin Spencer, EVP, Chief Business Officer of Nicox.** "*We expect the potential of NCX 470 can be harnessed by establishing strong commercial partnerships which can support the pricing and reimbursement work necessary for a successful launch, and developing additional clinical and nonclinical support for the therapeutic profile of NCX 470, such as the data we aim to generate on NCX 470's potential retinal benefits and the results from the ongoing Denali trial.*"

Program of studies to demonstrate potential retinal benefits of NCX 470

"*We have consulted with Key Opinion Leaders with expertise in the damage caused in the retina by glaucoma, including some of our Glaucoma Clinical Advisory Board members, who are enthusiastic about the potential of NCX 470 in this area. With their expert knowledge, we have outlined a program of nonclinical and clinical studies to explore the activity of NCX 470 in the retina,*" said **Doug Hubatsch, EVP, Chief Scientific Officer at Nicox**. "*These studies are expected to generate nonclinical and clinical data within the next 12 to 18 months to support the differentiation of NCX 470.*"

The program of studies is planned to include evaluation of the effect of NCX 470 on ocular perfusion pressure through Episcleral Venous Pressure (EVP) and Optical Coherence Tomography (OCT) measurements of retinal vessels in which NCX 470's ability to lower episcleral venous pressure as well as enhance outflow through the trabecular meshwork will be evaluated. Additionally, retinal blood vessel density will be studied in a separate clinical trial using OCT-angiography to fully understand effects on retinal blood flow. Together, these studies 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.

The planned initiation of these clinical studies is included in the Company's cash runway to mid-November, 2023, however the studies are not expected to be completed by that date and will require additional funding.

Rationale for retinal benefit and the role of nitric oxide (NO)

Elevated IOP is the main risk factor in glaucoma; however, a variety of IOP-independent risk factors, including ischemia (inadequate blood supply), contribute to damage of the optic nerve head and the retina, ultimately causing vision loss. NO is a potent vasodilator, and Nicox has previously demonstrated[1] a partial reversal of the ischemic effects on ocular hemodynamics and retinal dysfunction by administering a Nicox NO-donating compound. We also recently reported[2] nonclinical results in an ischemia/reperfusion model suggesting that NCX 470 improves ocular perfusion and retinal function in damaged eyes compared to vehicle and therefore may have therapeutic properties beyond lowering of IOP.

About NCX 470

NCX 470 is a novel, nitric oxide (NO)-donating bimatoprost eye drop that leverages the potent IOP-lowering effects of NO and prostaglandin analogs (PGAs). NCX 470 incorporates Nicox's proprietary NO-donating research platform and bimatoprost in a single molecule. NCX 470 is designed to release bimatoprost and NO into the eye to lower IOP by two pathways in patients with open-angle glaucoma or ocular hypertension. NO is a well-known, small, naturally-occurring signaling molecule that plays a key role in the regulation of IOP through activation of soluble guanylate cyclase (sGC). NO brings additional IOP-lowering efficacy by enhancing aqueous humor drainage from the eye via a different mechanism of action than that engaged by prostaglandin analogs. Bimatoprost, marketed under the brand name LUMIGAN® by AbbVie, Inc., is the leading branded PGA. PGAs are the most widely used class of drugs for IOP-lowering in patients with open-angle glaucoma or ocular hypertension.

NCX 470 is currently in Phase 3 development for the lowering of intraocular pressure in patients with open-angle glaucoma or elevated intraocular pressure. The program consists of two trials, Mont Blanc and Denali. Topline results from the Mont Blanc trial were reported on October 31, 2022. The similarly designed, ongoing, second Phase 3 trial, Denali, is being conducted at clinical sites in the U.S. and China, with topline results expected after 2024. The Denali trial also includes a long term safety extension through to 12 months, and is being jointly conducted and equally financed with our Chinese partner, Ocumension Therapeutics.

The Mont Blanc and Denali trials have been designed to fulfill the regulatory requirements to support New Drug Application (NDA) submissions in the U.S. and China and will also provide data for other countries accepting the same clinical data package for approval. The design of the efficacy part of the Denali trial is

[1] Impagnatiello, F. *et al*, Br. J. Ophthalmol. 96:757–761, 2012
[2] Bastia, E.J Ocul Pharmacol Ther. 2022, 38: 496-504

identical to that of Mont Blanc, however there is no guarantee that the results will be the same. 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. Should NCX 470 be developed for other territories, for example Europe or Japan, there may be additional requirements.

Corporate Update

Nicox is focused on completing the analysis of the Mont Blanc data, which will be presented at key upcoming scientific congresses, the ongoing NCX 470 Denali Phase 3 glaucoma trial and investigating the potential retinal benefits of NCX 470 in a program of both nonclinical and clinical studies. In addition, research activities continue on NCX 1728, the lead candidate in a new class of molecules, the NO-donating phosphodiesterase-5 inhibitors in both IOP lowering and retinal protection.

Given that the Mont Blanc Phase 3 clinical trial of NCX 470 met its primary objective of non-inferiority to latanoprost, the Company has met the condition necessary to exercise its option to extend the period of interest-only payment of its existing Kreos debt by six months to January 1, 2024. Nicox may exercise this option at any time until August 1, 2023. If this option is not exercised, the interest only period will end on July 1, 2023.

The Company estimates that it is financed until mid-November 2023, and until mid-December 2023 assuming the extension of the interest only period of the existing Kreos debt, in both cases based on the development of NCX 470 alone.

About Nicox

Nicox SA is an international ophthalmology company developing innovative solutions to help maintain vision and improve ocular health. Nicox's lead program in clinical development is NCX 470, a novel nitric oxide-donating bimatoprost, for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The company is also conducting research on NCX 1728, a nitric oxide-donating phosphodiesterase 5 inhibitor, in intraocular pressure lowering and retinal conditions. NCX 4251, a novel, patented, ophthalmic suspension of fluticasone propionate nanocrystals for topical ocular application for dry eye disease, is being developed by Ocumension Therapeutics in China under an exclusive license agreement and is available for partnering elsewhere. Nicox generates revenue from VYZULTA® in glaucoma, licensed exclusively worldwide to Bausch + Lomb, and ZERVIATE® in allergic conjunctivitis, licensed in multiple geographies, including to Eyevance Pharmaceuticals, LLC (a wholly-owned subsidiary of Santen Pharmaceutical Co., Ltd.), in the U.S. and Ocumension Therapeutics in the Chinese and in the majority of Southeast Asian markets.

Nicox is headquartered in Sophia Antipolis, France, is listed on Euronext Paris (Compartment B: Mid Caps; Ticker symbol: COX) and is part of the CAC Healthcare, CAC Pharma & Bio and Next 150 indexes.

For more information on Nicox, its products or pipeline, please visit: www.nicox.com.

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Risks factors which are likely to have a material effect on Nicox's business are presented in the 3rd chapter of the '*Document d'enregistrement universel, rapport financier annuel et rapport de gestion 2021*' filed with the French Autorité des Marchés Financiers (AMF) on April 29, 2022 which is available on Nicox's website (www.nicox.com)

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