Press Release

Nicox Reports Achieving Primary Objective in Mont Blanc, the First Phase 3 Glaucoma Trial for NCX 470

- **Mont Blanc, the first of two Phase 3 trials for NCX 470, met the efficacy requirements for approval in the United States**
- **Daily dosing of NCX 470 0.1% met the primary efficacy objective of demonstrating non-inferiority to latanoprost 0.005%, with NCX 470 showing 8.0 to 9.7 mmHg intraocular pressure lowering from baseline**
- **NCX 470 0.1% was statistically superior to latanoprost 0.005% in intraocular pressure reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6 timepoints However the secondary efficacy objective, statistical superiority to latanoprost, was not achieved**
- **NCX 470 0.1% was well tolerated**

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Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced that once daily dosing of NCX 470 0.1% met the primary objective of non-inferiority in lowering intraocular pressure (IOP) compared to the standard of care, latanoprost 0.005%, in the 691-patient Mont Blanc Phase 3 clinical trial in patients with open-angle glaucoma or ocular hypertension. The IOP-lowering effect from baseline for NCX 470 was 8.0 to 9.7 mmHg vs. 7.1 to 9.4 mmHg for latanoprost (reduction in time-matched IOP at 8 AM and 4 PM across the week 2, week 6 and month 3 visits). In a pre-specified secondary efficacy analysis of time-matched change from baseline IOP, statistical superiority was not achieved, however the IOP reductions for NCX 470 were numerically greater than those for latanoprost at all 6 timepoints, and statistically significant ($p<0.049$) at 4 of the 6 timepoints. NCX 470, a novel nitric oxide (NO)-donating bimatoprost eye drop, is currently in a Phase 3 clinical program.

"*These results demonstrate that NCX 470 has a robust intraocular pressure lowering effect, with good tolerability, and that it clearly met the primary objective of the Mont Blanc Phase 3 trial. 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. We are continuing to examine the Mont Blanc data including a number of additional ongoing pre-specified analyses which are important to fully define the profile of NCX 470, as well as further exploring NCX 470's activity on retinal cell protection, beyond its intraocular pressure lowering properties.*" said **Andreas Segerros, Chief Executive Officer of Nicox**.

NCX 470 Glaucoma Mont Blanc Phase 3 Topline Results Summary

- IOP-lowering effect from baseline was 8.0 to 9.7 mmHg for NCX 470 vs. 7.1 to 9.4 mmHg for latanoprost (reduction in time-matched IOP at 8 AM and 4 PM across the week 2, week 6 and month 3 visits).
- Non-inferiority 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 intraocular pressure 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 an 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.

"*We would like to acknowledge and thank all patients, clinical investigators and their teams for their contributions to the Mont Blanc trial, particularly during the challenging COVID-19 pandemic period.*" **said Doug Hubatsch, Executive Vice President, Chief Scientific Officer of Nicox.**

NCX 470 Phase 3 Trials Designs

Mont Blanc is a randomized, multi-regional, double-masked, parallel group trial that evaluated the safety and efficacy of NCX 470 ophthalmic solution, 0.1% compared to latanoprost ophthalmic solution, 0.005% in 691 patients. Latanoprost is the most widely prescribed first-line therapy for open-angle glaucoma or ocular hypertension. The Mont Blanc trial enrolled 691 patients in 56 sites in the United States and one site in China. The primary efficacy evaluation 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.

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 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 non-clinical data will also be required to complete NDA submissions. Should NCX 470 be developed for other territories, for example Europe or Japan, there may be additional requirements.

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.

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.

Analyst coverage

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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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