Press Release

Nicox Announces Results of the Exploratory Whistler Phase 3b Glaucoma Trial

- **Several aqueous humor parameters stimulated by nitric oxide were statistically significant or trended in favor of NCX 470; likewise those that respond to prostaglandin analogs**
- **Episcleral venous pressure changes did not show a trend vs. placebo**
- **Safety profile is consistent with that of the first Phase 3 trial, Mont Blanc**
- **NCX 470 intraocular pressure lowering efficacy and safety have already been demonstrated in the Phase 3 glaucoma trial, Mont Blanc**
- **Timeline and planning for New Drug Application submissions remain on track**

May 14, 2025 – release at 7:30 am CET

Sophia Antipolis, France

Nicox SA (Euronext Growth Paris: FR0013018124, ALCOX), an international ophthalmology company, today announced the results of the Whistler Phase 3b exploratory clinical trial investigating the dual mechanism of action (nitric oxide and prostaglandin analog) of NCX 470 in intraocular pressure (IOP) lowering in healthy volunteers and ocular hypertensive patients.

"*We believe that the outcomes in favor of NCX 470 in several trabecular meshwork aqueous humour dynamics parameters* are *due to nitric oxide. These positive exploratory results suggest that further investigation may be warranted into the dual mechanism effect of NCX 470 on intraocular pressure."* said **Doug Hubatsch, Chief Scientific Officer of Nicox.** "*The therapeutic characteristics of NCX 470 demonstrated in the Phase 3 program so far shows that we have an approvable and differentiated asset with a promising clinical profile. We look forward to announcing the safety and efficacy results from our ongoing Phase 3 trial, Denali, expected in the third quarter of this year*."

The Whistler Phase 3b exploratory trial was a double-masked, placebo-controlled study designed to further our understanding of the action of NCX 470 ophthalmic solution, 0.1%, on various aqueous humor dynamic parameters in 18 healthy volunteers or subjects with ocular hypertension. Measurements were taken at baseline and after 8 days at 1 pm and, for some parameters, at 3 pm.

Changes in aqueous humor flow rate trended towards significance vs. placebo (p=0.072). Outflow facility was positive at 1 pm (p=0.081), significant at 3 pm (p=0.001), as was the diurnal outflow (p=0.004). We believe this change is due to the effect of nitric oxide on the trabecular meshwork[1]. IOP lowering and uveoscleral outflow were statistically significant at all timepoints measured, whilst episcleral venous pressure did not show a notable trend. These findings

[1] For examples of the role of nitric oxide on these parameters, see Dismuke WM, Liang J, Overby DR, Stamer WD. Concentration-related effects of nitric oxide and endothelin-1 on human trabecular meshwork cell contractility. Exp Eye Res. 2014;120:28–35 and Wiederholt M, Sturm A, Lepple-Wienhues A. Relaxation of trabecular meshwork and ciliary muscle by release of nitric oxide. Invest Ophthalmol Vis Sci. 1994;35:2515–2520.

support the dual mechanism of action for IOP lowering of NCX 470 through both the conventional (nitric oxide-stimulated) and the uveoscleral (prostaglandin-stimulated) pathways. The safety profile observed was consistent with that of the first Phase 3 trial, Mont Blanc.

The Whistler trial was an exploratory trial and is not a requirement for the submission of New Drug Applications for NCX 470 and therefore does not impact the development timeline. The patient population in the Whistler trial was primarily normotensive healthy volunteers with mean baseline IOPs of 16.6 mmHg and 16.9 mmHg for NCX 470 and placebo treated patients, respectively. This is not the same patient profile as in the Phase 3 glaucoma program. Safety and efficacy have already been demonstrated in the first Phase 3 clinical trial, Mont Blanc. The results of the Mont Blanc trial are available on the Company's website, www.nicox.com.

About NCX 470

NCX 470, Nicox's lead clinical product candidate, is a novel NO-donating bimatoprost eye drop, currently in Phase 3 clinical development for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. Results of Mont Blanc, the first of the two Phase 3 clinical trials, have been extensively published and are available on our website. The second Phase 3 clinical trial, Denali, is currently ongoing. The last American patient in Denali has completed their final visit, with Chinese patients completing theirs, and the results are expected in Q3 2025. Mont Blanc and Denali have been designed to fulfil the regulatory requirements for safety and efficacy Phase 3 trials to support NDA submissions in both the U.S. and in China, where NCX 470 is exclusively licensed to Ocumension Therapeutics. NCX 470 is also licensed exclusively to Kowa for Japan.

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 (bimatoprost grenod), a novel nitric oxide-donating bimatoprost eye drop, for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. Nicox also has a preclinical research program on NCX 1728, a nitric oxide-donating phosphodiesterase-5 inhibitor, with Glaukos. Nicox's first product, VYZULTA® in glaucoma, licensed exclusively worldwide to Bausch + Lomb, is available commercially in the U.S. and over 15 other territories. Nicox generates revenue from ZERVIATE® in allergic conjunctivitis, licensed in multiple geographies, including to Harrow, Inc. in the U.S., and Ocumension Therapeutics in the Chinese and in the majority of Southeast Asian markets.

Nicox, headquartered in Sophia Antipolis, France, is listed on Euronext Growth Paris (Ticker symbol: ALCOX) and is part of the CAC Healthcare index.

For more information www.nicox.com

Analyst coverage

H.C. Wainwright & Co	Yi Chen	New York, U.S.

The views expressed by analysts in their coverage of Nicox are those of the author and do not reflect the views of Nicox. Additionally, the information contained in their reports may not be correct or current. Nicox disavows any obligation to correct or to update the information contained in analyst reports.

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Risks factors which are likely to have a material effect on Nicox's business are presented in section 3 of the "*Rapport Annuel 2024*" which is available on Nicox's website (www.nicox.com).

Finally, this press release may be drafted in the French and English languages. If both versions are interpreted differently, the French language version shall prevail.

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