Press Release

Nicox's Positive Post Hoc Results from NCX 4251 Phase 2b Mississippi Trial Suggest Path Forward in Dry Eye Disease

- **A subgroup of patients in the Phase 2b Mississippi clinical trial showed greater responses to NCX 4251 compared to placebo in reducing their dry eye symptoms**
- **Statistical significance reached for a number of symptoms and approached significance for one sign**
- **Potential alternative development path for discussion with the FDA early 2022**
- **Dry eye market is estimated to be worth over $5 billion worldwide**

November 30, 2021 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced positive post hoc results from its Mississippi Phase 2b clinical trial suggesting that once-daily dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, is effective in reducing dry eye symptoms in a subgroup of patients. The new results show that, for a subgroup of patients scoring more highly for a key sign of dry eye, statistically significant improvements in a number of dry eye symptoms and improvements in one sign (p=0.0524) were seen. The top-line results from the trial, which did not meet the primary or secondary efficacy endpoints, were reported on September 23, 2021.

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 placebo 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. The next steps and timelines in the development of NCX 4251 will be announced following a meeting with the U.S. Food and Drug Administration, scheduled to take place at the beginning of 2022.

Michele Garufi, Chairman and Chief Executive Officer of Nicox, said *"Dry eye disease is reported in some 70-80% of patients with blepharitis. The positive impact of NCX 4251 on the multitude of symptoms associated with dry eye disease in a substantial subgroup of blepharitis patients in the trial provides a compelling rationale to explore a targeted approach to the future development of the program with the FDA. We believe that there is still a significant unmet medical need in dry eye disease which could be filled with an efficacious short-term treatment applied only once-daily"*

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 adverse events.

Mississippi was a Phase 2b clinical trial, which recruited 224 patients at multiple clinical centers in the U.S., the subpopulation described here comprises 123 patients (61 in placebo and 62 in NCX 4251), evaluating

once-daily dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, versus placebo in patients with acute exacerbations of blepharitis. The primary outcome measure 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. The study also explored two secondary outcome measures on signs and symptoms of dry eye.

About NCX 4251 and Blepharitis

NCX 4251, our novel patented ophthalmic suspension of fluticasone propionate nanocrystals, is in development as a targeted topical treatment of the eyelids for patients with acute exacerbations of blepharitis, a common eye condition characterized by eyelid inflammation, and potentially for dry eye. 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. We believe that this is the first time that fluticasone propionate is being developed for an ophthalmic indication, and that NCX 4251 is the first product candidate developed as a targeted topical treatment of the eyelids for patients with acute exacerbations of blepharitis and potentially for dry eye.

Nicox and Ocumension Therapeutics have entered into an exclusive license agreement for the development and commercialization of NCX 4251 for blepharitis in the Chinese market.

About Nicox

Nicox S.A. 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 prostaglandin analog, for lowering intraocular pressure in patients with glaucoma. The company is also developing NCX 4251, a proprietary formulation of fluticasone, for acute exacerbations of blepharitis. 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, in the U.S. and Ocumension Therapeutics in the Chinese and in the majority of South East 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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Edison Investment Research	Pooya Hemami	London, UK
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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 2020*' filed with the French *Autorité des Marchés Financiers* (AMF) on March 1, 2021 which are available on Nicox's website (www.nicox.com).

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