Press Release

Nicox Initiates Phase 2b Trial of NCX 4251, a Potential First-in-Class Treatment for Blepharitis

- **Mississippi Phase 2b trial will evaluate once-daily dosed NCX 4251 0.1% versus placebo in patients with acute exacerbations of blepharitis**
- **NCX 4251 has first-in-class potential, addressing the unmet medical need of patients with blepharitis**
- **If the primary endpoint is met, the trial could count as one of two pivotal trials required by the FDA for NDA submission in the U.S.**
- **Top-line results expected in Q4 2021**

December 15, 2020 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced the initiation of the Mississippi trial, a Phase 2b clinical trial of NCX 4251, evaluating once-daily dosed NCX 4251 0.1% versus placebo in patients with acute exacerbations of blepharitis. NCX 4251 is a novel patented ophthalmic suspension of fluticasone propionate nanocrystals. The direct application of NCX 4251 to the eyelids is designed to target the site of the inflammation whilst minimizing the intraocular exposure to the steroid fluticasone and the risk of developing increased intraocular pressure (IOP) and cataract. The first patient in the Mississippi trial was enrolled in the U.S. on December 14th, 2020.

Dr José Boyer, Vice President and Interim Head of R&D at Nicox, commented "*As agreed previously with the U.S. Food and Drug Administration, should NCX 4251 meet the primary efficacy endpoint for blepharitis, the Mississippi trial could represent the first of two pivotal trials needed to support a New Drug Application for the treatment of blepharitis in the U.S. The Mississippi trial is also designed to assess the impact of NCX 4251 on dry eye disease, paving the way for a potential future standalone Phase 3 program in this indication*".

The Mississippi trial is expected to randomize 200 patients at 5 to 10 clinical sites across the U.S. The primary outcome measure is the proportion of patients achieving complete cure in eyelid redness, eyelid debris and eyelid discomfort, the hallmark signs and symptoms of blepharitis, at Day 15. Secondary outcome measures also include signs and symptoms of dry eye disease. Top-line results of the Mississippi trial are currently expected in Q4 2021.

The safety and tolerability of NCX 4251 ophthalmic suspension 0.1% were evaluated in the Danube Phase 2 clinical trial, completed in late 2019. Nicox believes 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 eyelid for patients with acute exacerbations of blepharitis. Nicox estimates the market potential for treatment of acute exacerbations of blepharitis in the U.S., where there are currently no approved treatments, at more than $700 million annually, and expects it to reach over $1 billion by 2024.

Nicox continues to closely watch the spread of COVID-19 and its impact. Nicox does not currently anticipate delays to clinical timelines but is monitoring the situation and will provide updates if there is an impact on development projects and timelines.

NCX 4251 - Danube Phase 2 trial

NCX 4251 completed a U.S. multicenter, dose escalating, first-in-human, 36-patient Danube Phase 2 clinical trial which evaluated its safety and tolerability in patients with acute exacerbations of blepharitis. In the Danube Phase 2 trial, NCX 4251 met the primary objective of selecting the dose for further

development. Although the trial was not powered for efficacy, in the prospectively defined pooled analysis of once-daily (QD) and twice-daily (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 placebo with p = 0.047 for study eyes and p = 0.025 for combined study eyes and contralateral eyes). The NCX 4251 0.1% QD treatment was selected to advance into a larger Phase 2 clinical trial. The selected dose of NCX 4251 0.1%, also demonstrated promising efficacy in reducing signs and symptoms of dry eye disease. 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.

Following the Danube trial, a successful Type C meeting was held with the U.S. FDA, with agreement on Phase 2 trial designs for NCX 4251 in both acute exacerbations of blepharitis and the reduction of signs and symptoms of dry eye disease.

NCX 4251 is exclusively licensed to Ocumension Therapeutics for the Chinese market.

About NCX 4251 and Blepharitis

NCX 4251, our novel patented ophthalmic suspension of fluticasone propionate nanocrystals, is being developed as a targeted topical treatment of the eyelid for patients with acute exacerbations of blepharitis, a common eye condition characterized by eyelid inflammation. 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 extra ophthalmic indications, including asthma and allergic rhinitis, and it 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 eyelid for patients with acute exacerbations of blepharitis.

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, second-generation nitric oxide-donating bimatoprost 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

Bryan, Garnier & Co	Victor Floc'h	Paris, France
Cantor Fitzgerald	Louise Chen	New York, U.S.
H.C. Wainwright & Co	Yi Chen	New York, U.S.
Kepler Cheuvreux	Damien Choplain	Paris, France
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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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Forward-Looking Statements

The information contained in this document may be modified without prior notice. This information includes forward-looking statements. Such forward-looking statements are not guarantees of future performance. These statements are based on current expectations or beliefs of the management of Nicox S.A. and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Nicox S.A. and its affiliates, directors, officers, employees, advisers or agents, do not undertake, nor do they have any obligation, to provide updates or to revise any forward-looking statements.

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 2019*' filed with the French *Autorité des Marchés Financiers* (AMF) on March 6, 2020 which are available on Nicox's website (www.nicox.com) and as restated in the 4th chapter of the half yearly financial report as of June 30, 2020, which is also available on Nicox's website.

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