Press Release

Nicox's NCX 4251 Meets Primary Endpoint in Phase 2 Blepharitis Trial and Shows Promising Efficacy in Dry Eye Disease

- **First-in-human safety and tolerability Phase 2 clinical trial 'Danube' in 36 patients met primary objective of selecting the dose of NCX 4251 for further development**
- **NCX 4251 0.1% once daily (QD) treatment was selected to advance into larger Phase 2b clinical trial, subject to a meeting with the U.S. FDA in early 2020 and securing the necessary financial resources**
- **Selected dose demonstrated promising efficacy in reducing signs and symptoms of acute exacerbations of blepharitis, and reducing signs and symptoms of dry eye disease**

December 19, 2019 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced that NCX 4251, a novel patented ophthalmic suspension of fluticasone propionate nanocrystals, has met the primary objective of its U.S. multicenter, dose escalating, first-in-human, Phase 2 clinical trial (referred to as 'Danube') evaluating the safety and tolerability of NCX 4251 in patients with acute exacerbations of blepharitis.

The primary objective of the Danube clinical trial was to select the dose(s) of NCX 4251 to advance into the next stage of development. NCX 4251 0.1% once daily (QD) treatment was selected to advance into a larger Phase 2b clinical trial, pending the outcome of a meeting with the U.S. Food and Drug Administration (FDA) in early 2020. Both once daily and twice daily (BID) NCX 4251 0.1% were well tolerated and there were no treatment related serious adverse events or adverse events of intraocular pressure (IOP) elevation, the most common side effect of topical ophthalmic steroids.

The selected dose also demonstrated promising efficacy against exploratory endpoints in the study in reducing the signs and symptoms of dry eye disease.

Tomas Navratil, PhD, Executive Vice President, Head of Development of Nicox, said, *"The delivery of these encouraging blepharitis results on time demonstrates that Nicox is executing on its R&D strategy to potentially have two advanced clinical programs in 2020. We are also pleased by NCX 4251's encouraging trends in the reduction of the signs and symptoms of dry eye disease, an important market in which NCX 4251 may have a benefit for treatment of the acute exacerbations of dry eye disease and as an induction therapy prior to the initiation of chronic dry eye treatment. We plan to discuss next steps for NCX 4251 with the U.S. FDA early next year and to secure the financial resources to accelerate its development."*

NCX 4251 Danube Phase 2 Trial Summary

- All patients in the once daily (n=10 for NCX 4251 and n=5 for placebo) and twice daily (n=10 for NCX 4251 and n=11 for placebo) cohorts successfully completed the 14-day dosing period followed by a 14-day safety evaluation period.

- 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.

- Although the study was not powered for efficacy, in the prospectively defined pooled analysis of QD and 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 eyes and contralateral eyes).

- Exploratory analyses of signs and symptoms of dry eye disease, including symptom evaluation using visual analog scale and sign evaluation based on fluorescein staining, revealed encouraging reduction from pre-study baselines.

NCX 4251 is a novel patented ophthalmic suspension of fluticasone propionate nanocrystals which Nicox believes is the first product candidate developed as a targeted topical treatment of the eyelid margin for patients with acute exacerbations of blepharitis. Blepharitis is a common eye condition characterized by eyelid inflammation.

About NCX 4251

NCX 4251 is a novel patented ophthalmic suspension of fluticasone propionate nanocrystals which is being developed as a targeted topical treatment of the eyelid margin for patients with acute exacerbations of blepharitis. 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 margin for patients with acute exacerbations of blepharitis. Thus we believe that NCX 4251 may be able to achieve first-in-class status as a treatment for this indication. Blepharitis is a common eye condition characterized by eyelid inflammation. NCX 4251 is being developed for application via eyelid applicator to the eyelid margin, applied directly to the site where the disease originates and thereby potentially minimizing penetration of the drug through the cornea which can lead to the damaging side effects such as intraocular pressure (IOP) increase found with current topical steroids.

Fluticasone propionate, the active ingredient in NCX 4251, which has not previously been approved in a topical formulation for use in ophthalmology, has an affinity for the glucocorticoid receptor which is approximately ten times greater than dexamethasone, a corticosteroid commonly used in ophthalmology. Fluticasone is a glucocorticoid with potent anti-inflammatory properties that has been approved in numerous drug products over the past 20 years for the treatment of various indications including dermatology, rhinitis and asthma.

Blepharitis – an untapped market

Blepharitis is a condition in which the margins of the eyelids become red and swollen and may contain dandruff like matter. Of patients seen by ophthalmologists and optometrists, 37% and 47%, respectively, present with signs of the disease.

There is currently no FDA-approved prescription product solely indicated for blepharitis, which limits our ability to estimate prevalence and market size. There are, however, antimicrobial and antibiotic products, such as ointments and eye drops, indicated for the treatment of blepharitis, as well as other conditions. Treatment options also include lid scrubs, topical ophthalmic steroids, topical ophthalmic antibiotics and topical ophthalmic antibiotic/steroid combinations. We estimate that the market for treatment of acute exacerbations of blepharitis in the U.S. alone may be more than $700 million, rising to over $1 billion by 2024.

About Nicox

Nicox S.A. is an international ophthalmology company developing innovative solutions to help maintain vision and improve ocular health. By leveraging our proprietary expertise in nitric oxide (NO) donation and other technologies, we are developing an extensive portfolio of novel product candidates that target multiple ophthalmic conditions, including glaucoma. Our portfolio has three programs in development including NCX 470, a novel, second-generation NO-donating bimatoprost analog, for intraocular pressure lowering, based on our proprietary NO-donating research platform and NCX 4251, a proprietary formulation of the well-established molecule fluticasone, for acute exacerbations of blepharitis. Our research activities are focused on novel future generation NO-donors including NO-donating phosphodiesterase-5 (PDE5) inhibitors and NO-donating soluble guanylate cyclase (sGC) stimulators (in partnership with Cyclerion). In addition, we have two ophthalmology assets that have been approved by the U.S. Food and Drug Administration (FDA); VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%, exclusively licensed worldwide to Bausch + Lomb, a Bausch Health Companies Inc. company, and commercialized in the U.S. by Bausch + Lomb since December 2017, as well as ZERVIATE™ (cetirizine ophthalmic solution), 0.24%, exclusively licensed in the U.S. to Eyevance Pharmaceuticals, LLC.

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	Hugo Solvet	Paris, France
Cantor Fitzgerald	Louise Chen	New York, U.S.
H.C. Wainwright & Co	Yi Chen	New York, U.S.
Oppenheimer & Co	Hartaj Singh	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.

Contacts

Nicox
Gavin Spencer
Executive Vice President, Chief Business Officer
& Head of Corporate Development
T +33 (0)4 97 24 53 00
communications@nicox.com

Investors & Media
United States & Europe
LifeSci Advisors, LLC
Hans Herklots
T +41 79 598 71 49
hherklots@lifesciadvisors.com

Media
France
LifeSci Advisors, LLC
Sophie Baumont
M +33 (0)6 27 74 74 49
sophie@lifesciadvisors.com

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Risks factors which are likely to have a material effect on Nicox's business are presented in the 4th chapter of the '*Document de référence, rapport financier annuel et rapport de gestion 2018*' filed with the French *Autorité des Marchés Financiers* (AMF) on March 6, 2019 which are available on Nicox's website (www.nicox.com).

Nicox S.A.
Drakkar 2
Bât D, 2405 route des Dolines
CS 10313, Sophia Antipolis
06560 Valbonne, France
T +33 (0)4 97 24 53 00
F +33 (0)4 97 24 53 99