## Press Release

# Nicox provides clinical and regulatory update for NCX 470 for IOP lowering

- **Positive pre-IND meeting with FDA completed**
- **Expect to file IND in Q4 2017**
- **First-in-Human Phase 2 clinical study expected to start in Q1 2018**

January 24, 2017
Sophia Antipolis, France

**Nicox S.A.** (Euronext Paris: FR0013018124, COX), the international ophthalmic R&D company, today provided certain regulatory and clinical updates for NCX 470, its novel nitric oxide (NO) donating bimatoprost analog being developed for intraocular pressure (IOP) lowering. Increased IOP is one of the principal risk factors of open-angle glaucoma and ocular hypertension.

Nicox held a pre-Investigational New Drug (IND) meeting with the U.S. Food and Drug Administration (FDA) at the end of 2016. Based on the feedback from this meeting, Nicox is finalizing the design of a first-in-human trial for NCX 470 which will be a Phase 2 multi-center, investigator masked, 28-day, parallel group, dose-finding study in adult subjects with elevated IOP due to open-angle glaucoma or ocular hypertension. Multiple doses of NCX 470 will be compared in safety and efficacy to bimatoprost. The primary endpoint of the study is the mean reduction in IOP, and the objective is to identify the appropriate safe and effective dose of NCX 470 to be taken into Phase 3 studies. Recruitment of subjects is expected to begin in early 2018, subject to IND filing and acceptance[1], and the study is expected to take approximately 1 year to complete.

**Dr. Mike Bergamini, EVP and Chief Scientific Officer of Nicox commented,** *"All pharmacological treatments currently available and in advanced stages of development for glaucoma target the lowering of IOP as each additional mmHg reduction results in a 10 to 20% reduced risk of vision loss. NCX 470 has been developed using a similar NO-donation platform to latanoprostene bunod, the Nicox molecule being developed for IOP lowering by our partner Bausch + Lomb, which is expected to launch in the U.S. in mid-2017. We believe the clinical results of latanoprostene bunod validate the mechanism of action of NO-donating prostaglandin analogs, and we expect NCX 470 to also demonstrate considerable IOP lowering activity. Our R&D team is currently finalising the necessary pre-IND activities to support filing of the IND in Q4 this year, allowing us to enroll subjects directly into Phase 2 in early 2018."*

*"NCX 470 is the second candidate molecule for which we have recently announced plans to move into the clinic within the next 12 months, further solidifying our broad pipeline of programs in ophthalmology,"* **said Michele Garufi, Chairman and Chief Executive Officer of Nicox, adding,** *"As with latanoprostene bunod, NCX 470 has been generated by our dedicated and experienced team of researchers who are leaders in studying the role of NO in the eye. In addition to our clinic-ready programs, we are working on other new and innovative NO-based projects currently focused on IOP lowering and glaucoma, including our proprietary next-generation of stand-alone NO-donors."*

### About NO and NO-donating drugs

Nitric oxide (NO) is an endogenous cell-signalling molecule of fundamental importance in physiology. Nicox has developed a world-leading position in the therapeutic application of NO-donating compounds, based on a strong research platform which creates New Molecular Entities (NMEs). These compounds, known as NO-donors, are designed to donate nitric oxide with a sustained pharmacological effect at tissue level aiming at avoiding the drawbacks related to the rapid burst of NO associated with traditional nitrates. NO and other

messengers involved in NO-mediated signalling are present in ocular tissues, and NO plays a role in the regulation of IOP, believed to be by improving outflow of aqueous humor from the eye through the trabecular meshwork/Schlemm's canal, a mechanism which is complementary to that of prostaglandin analogs.

## About NCX 470

NCX 470 is a proprietary novel nitric oxide (NO) donating bimatoprost analog discovered in Nicox's Research Laboratories. Nicox owns worldwide rights to NCX 470.

In three preclinical models of glaucoma and ocular hypertension, NCX 470 appeared well-tolerated and more effective than equimolar bimatoprost in reducing intraocular pressure (IOP)[2]. Notably, in a preclinical model in which prostaglandin analogs are known to be inactive, NCX 470 lowered IOP suggesting that its nitric oxide-donating moiety produces an IOP-lowering effect. Bimatoprost, marketed under the brand name Lumigan®[3], is one of the leading products in the class of prostaglandin analogs, the most widely used class of IOP lowering drugs. Based on the positive Phase 3 results for latanoprostene bunod and increased interest in the potential of nitric oxide (NO)-donors in ophthalmology, Nicox's Board of Directors selected NCX 470 as the lead follow-on glaucoma candidate for internal development.

## About glaucoma

Glaucoma is a group of ocular diseases in which the optic nerve is injured, leading to the loss of the peripheral visual field and can eventually lead to blindness if not treated. Glaucoma is frequently linked to abnormally high pressure in the eye, due to blockage or malfunction of the eye's drainage system. In 2010, open-angle glaucoma (the most common form of glaucoma) was estimated to affect 8 million individuals in the 7 worldwide major markets (US, Japan, UK, France, Germany, Italy, Spain)[4].

**Notes:**

1. Once an IND has been filed, the FDA has 30 days to notify the sponsor of any questions they have. In the absence of questions, or once any questions from the FDA have been resolved, the sponsor may start the clinical study detailed in the IND
2. Impagnatiello F, Bastia E, Toris CB, Krauss AH, Prasanna G, Ongini E, NCX 470, a nitric oxide (NO)-donating bimatoprost lowers intraocular pressure in rabbits, dogs and non-human primate models of glaucoma. Abstract No. 5809. Presented at ARVO 2015.
3. Lumigan is a registered trademark of Allergan, Inc
4. The Ophthalmic Pharmaceutical Market Outlook to 2016 – Business Insight, Sept 2011, BI00042-019

## About Nicox

Nicox is an international ophthalmic R&D company utilizing innovative science to maintain vision and improve ocular health. By leveraging its proprietary expertise in nitric oxide donation and other technologies, the Company is developing an extensive portfolio of novel therapies that target multiple ophthalmic conditions, including glaucoma. Nicox currently has two products at the pre-approval stage with the U.S. Food and Drug Administration (FDA) and a promising pipeline including next-generation stand-alone nitric-oxide donors, with the potential to treat a range of ophthalmic indications. 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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| Invest Securities | Martial Descoutures | Paris, France |
| Gilbert Dupont | Damien Choplain | Paris, France |
| Stifel | Olivia Manser | London, UK |

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## Upcoming financial and business conferences

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| January 26 | Invest Securities Biomed Event | Paris, France |
| March 6-8 | Cowen and Company 37th Annual Healthcare Conference | Boston, US |
| April 4-5 | Needham's 16th Annual Healthcare Conference | New York, US |

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