Press Release

Nicox Selects Development Candidate in a New Class of NO-mediated Intraocular Pressure (IOP) Lowering Agents

- **Nicox expands internal pipeline with third innovative program**
- **The new class of compounds combines two converging cellular mechanisms with the aim of achieving an effective and sustained control of intraocular pressure (IOP) in glaucoma patients**
- **Previously disclosed[1,2] data demonstrate the potential of this new class for lowering IOP**

October 23, 2020 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced that it has selected a new development candidate, NCX 1728, from its proprietary research program focused on nitric oxide (NO)-mediated IOP lowering agents. An analog of this molecule has demonstrated[1] positive results in ocular hypertensive non-human primates compared to travoprost 0.1%, a prostaglandin analog. Prostaglandin analogs are the standard of care for IOP lowering therapies.

Nicox owns all exclusive worldwide rights to NCX 1728. Further optimization of the ophthalmic formulations of NCX 1728 will continue prior to initiating formal pre-Investigational New Drug (IND) tests required for the filing of an IND application.

Michele Garufi, Chairman and Chief Executive Officer of Nicox commented "*We are very proud to announce the selection of this new drug candidate, NCX 1728, which becomes our third in-house development program. NCX 1728 is the first in a new class of molecules combining the clinically proven effects of nitric oxide with phosphodiesterase-5 inhibition, which has been shown to enhance the efficacy and the duration of nitric oxide-mediated effects.*"

NCX 1728 was invented in Nicox's Bresso (Milan, Italy) Research Laboratories using the Company's proprietary NO-donating research platform, which has enabled the development of a leading scientific and strategic position in the therapeutic application of NO-donating compounds.

NO-mediated IOP lowering agents

It has been established that NO plays a key role in the regulation of IOP and can be linked with other pharmaceutical agents, as is the case with our lead clinical development candidate NCX 470, a second generation NO-donating prostaglandin analog, and the first generation product, VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%. VYZULTA is exclusively licensed worldwide to our partner Bausch + Lomb, who is commercializing it in the U.S. and Canada. The effect of NO on IOP lowering may be further increased or prolonged by phosphodiesterase-5 (PDE5) inhibitors, which inhibit the degradation of cyclic guanosine monophosphate (cGMP), a key intracellular messenger that is produced as a result of stimulation by NO.

NCX 1728 is the first in a new class of compounds where NO-mediated effects are enhanced by concomitant action of PDE5 inhibition within the same molecule. Data presented[2] on this class at the 2019 Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO) show statistically significant IOP changes compared to vehicle in laser-induced ocular hypertensive non-human primates. Additional data recently published[1] showed that a molecule of this class reduces IOP to a similar extent but with a faster onset of action when compared to travoprost.

Nicox is terminating the research collaboration with Novaliq GmbH concerning their water-free enabling EyeSol® technology since NCX 1728 has been selected and will be developed using an in-house, proprietary formulation.

References:

1. Impagnatiello F., Navratil T., Toris C.B., Bergamini M.V.W., et al., Intraocular pressure (IOP) reduction elicited with NCX 1741, a dual acting nitric oxide (NO) and phosphodiesterase type-5 (PDE5) inhibitor or travoprost in a non-human primate model of ocular hypertension and glaucoma *Investigative Ophthalmology & Visual Science* 2020*, Vol.61, 2786*
2. Impagnatiello F., Bastia E., Toris CB et al., NCX 1741, a novel NO-donating derivative of the phosphodiesterase-5 inhibitor avanafil, reduces IOP in models of ocular hypertension and glaucoma", Impagnatiello F., Bastia E., Toris C., Fan S., Brambilla S., Galli C., Almirante N., Bergamini M.V.W. *Investigative Ophthalmology & Visual Science* 2019, Vol.60, 3770.

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.

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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 2019*' filed with the French *Autorité des Marchés Financiers* (AMF) on March 6, 2020 which are available on Nicox's website (www.nicox.com).

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