

Press Release

Nicox Focuses Research Activities on Novel NO-Donating PDE5 Inhibitors for Glaucoma and Enters into Collaboration with Novaliq on Innovative Topical Ophthalmic Formulations

- Encouraging preclinical efficacy data on NO-donating PDE5 inhibitors
 - Focusing of research activities on the most promising new pharmacologic classes
 - Collaboration with Novaliq to access novel formulation technology for these new compounds
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Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced that it will be focusing its research activities on topical nitric oxide (NO)-donating phosphodiesterase-5 (PDE5) inhibitors and soluble guanylate cyclase (sGC) stimulators. As part of this focus, Nicox has entered into a research collaboration with **Novaliq GmbH** for the development of novel topical ophthalmic formulations of Nicox's NO-donating PDE5 inhibitors based on Novaliq's water-free enabling EyeSol® technology, for lowering intraocular pressure (IOP).

Michele Garufi, Chairman and Chief Executive Officer of Nicox, said, *"We have been impressed by Novaliq's ability to successfully combine existing molecules and new chemical entities with their EyeSol® technology. It uses a novel class of excipient that offers an opportunity to create unique formulations for the development of our NO-donating PDE5 inhibitor new chemical entities as innovative intraocular pressure lowering drug candidates. These novel formulations could potentially have multiple benefits, including improved ocular comfort and enhanced drug delivery performance with no antimicrobial preservative."*

"There are few new chemical entities in development for glaucoma patients, and the Nicox team is clearly at the forefront of the development of novel mechanisms of action for the lowering of intraocular pressure," said Dr. Christian Roesky, Chief Executive Officer of Novaliq. "Our EyeSol® technology has already successfully proved itself in multiple ophthalmic clinical studies and the partnership with Nicox allows us to bring together two novel technologies for innovation in the demanding field of glaucoma."

In this collaboration, Novaliq is developing and characterizing novel formulations for lead series of the NO-donating PDE5 inhibitor new chemical entities using its EyeSol® technology. If successful, Nicox will be testing the novel topical ophthalmic formulations of NO-donating PDE5 inhibitors for IOP lowering activity in established pre-clinical models. Newly developed intellectual property from the collaboration will be jointly owned.

Focusing of Nicox Research

Nicox's research team has recently generated encouraging pre-clinical data that have compelled the Company to focus its research activities on the topical delivery of its future generation of NO-donors that combine NO-release with other mechanisms of action to potentially lower IOP. These programs include the NO-donating PDE5 inhibitors, as well as the NO-donating sGC stimulators in partnership with Ironwood. The Company intends to disclose some of the new data at key upcoming ophthalmology

conferences in 2019. As a result of this new focus, Nicox will discontinue its research collaboration with Re-Vana, as well as its work on stand-alone NO-donors. Whilst the collaboration with Re-Vana met its objectives, the decision is strategic and not related to the quality of the Re-Vana technology, nor the professionalism of the Re-Vana Therapeutics team.

As of January 1, 2019, Mike Bergamini, Ph.D., in a new role of Chief Scientific Advisor, will provide scientific advice to the Company as well as supporting Nicox's NO-donating research activities.

Future Generation NO-donors using sGC stimulation and PDE5 inhibition in the eye

We are actively researching NO-donating compounds of different chemical and pharmacological classes from those previously evaluated, both in-house and through our collaboration with Ironwood, in order to add NO donation to their existing mechanism of action (MOA) and thus potentially enhancing the IOP lowering and other desirable pharmaceutical properties of these classes of molecules. Some of these are new therapeutic agent classes targeting conventional outflow through the trabecular meshwork by combining NO release with other pharmacological actions. These new therapeutic agent classes include NO-donating sGC stimulators and NO-donating PDE5 inhibitors. We expect to be able to announce a preclinical candidate from one of these programs in the next 18 months.

NO is present in ocular tissues, together with other components involved in the NO signaling cascade via the activation of sGC. The activation of sGC leads to the synthesis of cyclic guanosine monophosphate (cGMP) and an increase in the concentration of cGMP in the trabecular meshwork. This increase is followed by the relaxation of the trabecular meshwork and increased outflow of the aqueous humor from the anterior segment of the eye through the conventional outflow pathway. All of the foregoing lead to IOP lowering. The effect of NO in the sGC signaling cascade can be further increased or prolonged by sGC stimulators and/or by PDE5 inhibitors.

sGC stimulators and NO interact synergistically on sGC which result in greater cGMP production, as compared to the cGMP production that results from exposure to either sGC stimulators or NO alone. Further, PDE5 inhibitors inhibit phosphodiesterase type 5, a key enzyme that degrades cGMP to inactive guanosine monophosphate (GMP). This inhibition of PDE5 prevents the conversion of cGMP to inactive GMP which prolongs the duration of action of cGMP on the trabecular meshwork following the activation of sGC by NO.

About EyeSol®

As the first water-free enabling technology for ophthalmology products, EyeSol® enhances traditionally water-insoluble drugs. EyeSol® is based on specific semi-fluorinated alkanes (SFAs). These compounds have the same refractive index as water and are transparent, inert, non-toxic, amphiphilic liquids that can formulate lipophilic and large molecules. Due to their low surface tension and viscosity, SFAs dispense as a low volume drop that does not stimulate blinking or reflex tearing.

Being water-free, EyeSol® products avoid oxidative reactions that might degrade active pharmaceutical ingredients, thus improving product stability. In addition, the water-free EyeSol® technology does not permit microbial growth, and therefore it allows manufacturing of antimicrobial preservative-free formulations in multi-dose containers.

About Novaliq

Novaliq is a pharmaceutical company focusing on the development and commercialization of first- and best-in-class ocular therapeutics based on EyeSol®, the worldwide first water-free technology for ophthalmology. With an initial focus on dry eye disease (DED), Novaliq offers an industry-leading portfolio addressing today's unmet medical needs of millions of patients with eye diseases: Novaliq's lead assets in late-stage clinical development are CyclASol® and NOV03: CyclASol® is an anti-inflammatory and immune-modulating drug for the treatment of DED with a demonstrated early onset of action and an excellent tolerability. NOV03 is the first drug addressing evaporative DED associated with meibomian gland dysfunction (MGD). NovaTears® water-free eye drops for dry eye have CE Marking and are commercialized in Australia/New Zealand by AFT Pharmaceuticals and in Europe as EvoTears® by Ursapharm.

Novaliq is headquartered in Heidelberg, Germany and has also an office in Cambridge, MA, USA. The long-term shareholder is dievini Hopp BioTech Holding, an active investor in Life and Health Sciences companies. More on Novaliq at www.novaliq.com.

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 includes three programs in development including NCX 470 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 Ironwood). 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 Eyevence Pharmaceuticals.

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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Upcoming financial and business conferences

January 22, 2019	Invest Securities BioMed Event	Paris, France
February 12, 2019	European Midcap Event	Frankfurt, Germany
March 19-20, 2019	Oppenheimer's 29th Annual healthcare Conference	New York, U.S.
April 7-9, 2019	H.C. Wainwright Global Life Sciences Conference	London, UK

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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 2017*' filed with the French *Autorité des Marchés Financiers* (AMF) on March 19, 2018 which is available on Nicox's website (www.nicox.com).

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