Press Release

Nicox Reports Positive Results of Secondary Analyses from Phase 2 Trial Further Highlighting Potential of NCX 470 in Glaucoma

- **NCX 470 0.065% produced significantly superior intraocular pressure (IOP) lowering compared with latanoprost 0.005% in secondary analyses**
- **NCX 470 showed improved IOP lowering with each incremental concentration of NCX 470 tested, setting the stage for potentially further IOP lowering at a higher dose**
- **Phase 3 clinical program expected to be initiated in Q2 2020 with 0.065% and 0.1% doses, pending End-of-Phase 2 meeting with U.S. Food and Drug administration (FDA)**
- **Independent market research suggests NCX 470 with the present product profile could capture at least 25% of existing branded U.S. first-line therapy market, and a larger share with higher IOP reduction**

October 22. 2019 – release at 7:30 am CET
Sophia Antipolis, France

Nicox S.A. (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced the results of secondary analyses of its Dolomites Phase 2 trial with NCX 470 for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension. Positive top-line results were reported on October 2. 2019.

Michele Garufi, Chairman and Chief Executive Officer of Nicox, said, "*The secondary analyses we report today provide further strong support to the compelling clinical potential of NCX 470 in the treatment of ocular hypertension and glaucoma. Furthermore, the primary market research we have conducted in the U.S. via an independent agency already indicates the clear commercial opportunity of NCX 470.*"

Tomas Navratil, Ph.D., EVP and Head of Development, stated, *"As the next step, in our End-of-Phase 2 meeting with the U.S. FDA early next year, we intend to propose conducting our Phase 3 trials with 0.065%, the highest concentration used in the Dolomites trial, and a 0.1% concentration. This higher concentration has the potential for additional incremental improvement in IOP lowering, thus further enhancing the clinical and commercial profile of NCX 470."*

In the Dolomites trial, NCX 470 met the primary endpoint of non-inferiority and also demonstrated statistical superiority to latanoprost, the U.S. market leader in prostaglandin analog prescriptions, in multiple pre-specified analyses, with a 7.6 to 9.8 mmHg IOP reduction from baseline.

Key Points from Additional Analysis of Dolomites Trial

- All doses of NCX 470 (0.021%, 0.042%, and 0.065%) met pre-specified primary efficacy endpoint of non-inferiority to latanoprost for reduction from baseline in mean diurnal IOP at Day 28.
- Dose dependent IOP reduction from baseline in mean diurnal IOP at Day 28 showed improved IOP lowering with each incremental concentration of NCX 470 tested, thus creating the potential for additional IOP lowering with a higher concentration of NCX 470 which, subject to FDA agreement, we intend to test in Phase 3 clinical trials.
- In a responder analysis, 37% of patients demonstrated an IOP reduction of ≥ 2 mmHg vs. the mean IOP reduction with latanoprost, and 27% of patients for ≥ 3 mmHg.

- NCX 470 was well tolerated. The most frequently reported adverse event was conjunctival hyperemia in 16.8% of the NCX 470 (0.065%) patients vs. 6.5% of latanoprost patients; most of these events were rated as mild. There were no drug-related serious adverse events and no evidence of treatment-related systemic effects.

For the comprehensive results, please see the Appendix to this Press Release.

Market Research

- Independent market research on multiple potential profiles for NCX 470 was carried out with 40 interviews with U.S. ophthalmology key opinion leaders, high volume prescribers including ophthalmologists and optometrists, and third-party payers.
- Profiles varied by increasing superiority of IOP reduction compared to latanoprost.
- There is an opportunity for an impactful product with any of the three profiles tested and the market potential increased with the magnitude of IOP reduction. The profile closest to that of NCX 470 (0.065%) observed in the Phase 2 trial had the potential to capture at least 25% of existing branded U.S. first-line therapy glaucoma market by value.

For the comprehensive details of the Market Research, please see the Appendix to this Press Release.

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
H.C. Wainwright & Co	Yi Chen	New York, U.S.
Oppenheimer & Co	Hartaj Singh	New York, U.S.

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Upcoming Conferences

Bryan, Garnier & Co European Healthcare Conference	12 - 13 November, 2019	Paris
Actionaria	21 - 22 November, 2019	Paris

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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 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).

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APPENDIX

Comprehensive Clinical Results from the Dolomites Study

NCX 470 (0.021%, 0.042%, and 0.065%) met pre-specified primary efficacy endpoint of non-inferiority to latanoprost for reduction from baseline in mean diurnal IOP at Day 28.

- In pre-specified secondary efficacy analysis for reduction from baseline in mean diurnal IOP at Day 28, the mid and high doses of NCX 470 (0.042% and 0.065%) met the secondary efficacy endpoint of statistical superiority to latanoprost based on the study's pre-specified statistical analysis plan.
- IOP reduction from baseline in mean diurnal IOP at Day 28 was 7.8 mmHg for the 0.021% dose of NCX 470 (p-value for NCX 470 vs. latanoprost not statistically significant); 8.2 mmHg for the 0.042% dose of NCX 470 (p-value for NCX 470 vs. latanoprost=0.0281); and 8.7 mmHg for the 0.065% dose of NCX 470 (p-value for NCX 470 v. latanoprost=0.0009).
- Dose response of IOP reduction from baseline in mean diurnal IOP at Day 28 showed improved increase in IOP lowering with each incremental concentration of NCX 470 tested, thus creating the potential for additional IOP lowering with a higher dose of NCX 470 which, subject to FDA agreement, may be tested in future clinical trials.

Secondary Efficacy Analyses

- In additional pre-specified secondary efficacy analysis for reduction from baseline in mean diurnal IOP, NCX 470 (0.065%) met the secondary efficacy endpoint of statistical superiority to latanoprost at Day 7 (p=0.004) and Day 14 (p=0.0174), in addition to Day 28 (p=0.0009; described above)
- In pre-specified secondary efficacy analyses, the 0.065% dose of NCX 470 showed statistical superiority in IOP lowering as a reduction from baseline at all three time points (8 AM, 10 AM and 4 PM IOPs) on Day 28 compared with latanoprost, with the difference reaching up to 1.4 mmHg (p=0.0242 at 8 AM, p=0.0013 at 10 AM, and p=0.0016 at 4 PM).
- The IOP lowering effect as reduction from baseline at the three time points (8 AM, 10 AM and 4 PM IOPs) across Day 7, Day 14 and Day 28 ranged from 7.6 to 9.8 mmHg for the 0.065% concentration of NCX 470 compared with 6.3 to 8.8 mmHg for latanoprost.
- At Day 28, 44% of patients dosed with NCX 470 (0.065%) had a 1 mmHg or greater mean diurnal IOP reduction from baseline compared with the mean of 7.4 mmHg for the latanoprost group (p-value not significant); 37% of patients had 2 mmHg or greater reduction (p-value not significant); 27% had a 3 mmHg or greater reduction (p=0.0175); 16% had a 4 mmHg or greater reduction (p=0.0822); and 12% had a 5 mmHg or greater reduction (p=0.0150); compared with the mean for the latanoprost group. Furthermore, greater proportion of patients dosed with NCX 470 (0.065%) achieved a mean diurnal IOP reduction at Day 28 of 40% or greater (p=0.0287), 35% or greater (p=0.0393), 30% or greater (p-value not statistically significant), 25% or greater (p=0.0479) and 20% or greater (p=0.0115), compared with those dosed with latanoprost.

Safety and Tolerability

NCX 470 was well tolerated when dosed once daily for 28 days in patients with open-angle glaucoma or ocular hypertension. Only three out of the 433 patients in the trial discontinued due to an adverse event. The majority adverse events in the study were mild. The most frequent adverse event was conjunctival hyperemia, the majority of which were mild, in 16.8% of patients who dosed with the 0.065% dose of NCX 470 compared with 6.5% of patients who dosed with latanoprost. Notably, adverse events for conjunctival hyperemia plateaued at the 0.042% concentration, for which it was reported for 22.2% of patients. There were no treatment-related serious adverse events, and no evidence of treatment-related systemic side effects.

Market Research

In order to understand the potential clinical adoption of NCX 470 for glaucoma and to assess its reimbursement and revenue potential, an independent third party market research agency with extensive experience in the ophthalmology market assessment conducted an initial primary market research study in the United States in the first half of 2019. The market research was comprised of 40 interviews with U.S.

ophthalmology key opinion leaders, high volume prescribers including ophthalmologists and optometrists, and third party payers.

Multiple target product profiles of NCX 470 were tested with differentiation from each other by increasing superiority in IOP reduction compared to latanoprost 0.005%, based on a hypothetical statistically significant outcome in a head-to-head Phase 3 clinical study. The varying levels of efficacy in the three target product profiles tested were chosen based on the current U.S. FDA-approved therapies. For all three profiles, the safety and tolerability were identical and based on existing PGAs:

- A superiority to latanoprost similar to VYZULTA's published Phase 2 VOYAGER study was selected for the first profile but with a superior U.S. FDA label based on head-to-head Phase 3 studies vs. PGA for NCX 470
- A superiority to latanoprost similar to the published ROCKLATAN Phase 3 Mercury-1 clinical study at month three but with improved safety and tolerability vs ROCKLATAN was selected for the second profile
- A ~2 mmHg or better superiority to latanoprost was selected for the third profile.

The market research concluded that there was an opportunity for an impactful product with any of the three profiles tested and that the market potential increased with the size of the improved reduction in IOP:

- The VYZULTA-based product profile had peak U.S. net revenue potential of $230M (25% market share of the U.S. first-line therapy branded market).
- The Mercury-1 ROCKLATAN-based product potential but with improved safety and tolerability to ROCKLATAN had peak U.S. net revenue potential of $310M (35% market share of the U.S. first-line therapy branded market).
- The profile based on ~2 mmHg superiority to latanoprost had peak U.S. net revenue potential of $540M (60% market share of the U.S. first-line therapy branded market).

The above forecasts include estimations about the future growth of the market and assume an appropriate level of reimbursement is available.