Press Release

Nicox Reports 2021 Financial Results and First Quarter 2022 Financial Highlights and Provides Update on Key Programs and Milestones

- **NCX 470 Mont Blanc Phase 3 clinical trial in glaucoma at over 98% recruitment**
- **Development pathway for NCX 4251 in dry eye disease confirmed following meeting with the U.S. FDA**
- **First quarter 2022 U.S. prescriptions for VYZULTA® increased by 43% over first quarter 2021**
- **Cash position of €42.0 million as of December 31, 2021 and €35.1 million as of March 31, 2022, confirming the Company is financed to Q4 2023**

April 28, 2022 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced the financial and operating results for Nicox and its subsidiaries (the "Nicox Group") for the year ended December 31, 2021, as approved by the Board of Directors on April 27, 2022, along with a business update and financial highlights for the first quarter 2022, and provided an update on key upcoming milestones.

"*We are very pleased by the rapid progress of the NCX 470 Mont Blanc phase 3 trial and are eagerly expecting its completion which will mark a major inflexion point for our Company and a turning point in the development of drugs for the treatment of patients with open-angle glaucoma and ocular hypertension.*" said **Michele Garufi, Chief Executive Officer of Nicox**.

Key Upcoming Milestone

- **Mont Blanc Phase 3 clinical trial on NCX 470 in glaucoma:** recruitment advances more quickly than anticipated and thus topline results fully on track.

First Quarter 2022 and Recent Events and Pipeline Updates

Product candidates

NCX 470

- **NCX 470** is a novel nitric oxide (NO)-donating prostaglandin analog currently in a Phase 3 clinical program for the lowering of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.
- Owing to a better than expected enrollment rate in recent months, over 98% of the patients required to complete the **NCX 470** Mont Blanc Phase 3 clinical trial have been enrolled.
- Patient enrollment is continuing in both the United States (U.S.) and China in the ongoing Denali Phase 3 clinical trial on **NCX 470** in patients with open-angle glaucoma or ocular hypertension. Denali, which also includes a long-term safety extension, has been recruiting patients in the U.S. since November 2020. Approximately 670 patients are expected to be randomized at approximately 60 clinical sites in the U.S. and China, with approximately 80% of the patients to be

recruited in the U.S. and the remaining 20% of the patients to be recruited in China. The topline results will not be available by the end of 2023 as previously communicated due to several hurdles (including the COVID-19 pandemic situation in the U.S. and China). The Company will announce a new date for availability of the results when we have more visibility on the overall timelines of the trial.

- The Chinese National Intellectual Property Administration has granted Nicox a formulation patent for **NCX 470** in China to 2039. With the equivalent U.S. and European patents already granted, the formulation is now covered in most major global territories. NCX 470 is also covered by granted composition of matter patents.

NCX 4251

- **NCX 4251** is a novel, patented, ophthalmic suspension of fluticasone propionate nanocrystals in clinical development stage for dry eye disease.

- Following the encouraging *post hoc* results from the Mississippi Phase 2b clinical trial and a subsequent meeting with the U.S. Food and Drug Administration (FDA), the future development of **NCX 4251** will be focused on dry eye disease. The Mississippi *post hoc* results, reported on November 30, 2021, suggest that once-daily dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, is effective in reducing dry eye symptoms in patients who score more highly for a key sign of dry eye disease. The Company is currently exploring how to best advance the development of NCX 4251 in dry eye disease and will communicate its strategy at a future date.

- The Japanese Patent Office has granted a new patent expiring in 2040 for **NCX 4251**. Patent JP.7021301 covers ophthalmic suspensions comprising a specific form of fluticasone propionate nanocrystals and the method for manufacturing the ophthalmic suspensions. It complements the recent granting of a patent from the same family in Europe. Corresponding patent applications are under examination in the U.S., China and other territories.

Commercial Out-licensed Products

- **VYZULTA®** (latanoprostene bunod ophthalmic solution), 0.024% U.S. prescriptions[1] increased by 43% in the first quarter of 2022 compared to first quarter 2021, however revenue remained unchanged due to an increased level of rebates. As of December 31, 2021, VYZULTA, exclusively licensed worldwide to Bausch + Lomb, was commercialized in 7 territories: United States (2017), Canada (2019), Argentina (2020), Mexico (2020), Hong Kong (2020), Taiwan (2021) and Ukraine (2021). VYZULTA is also approved in 9 other countries, namely Brazil, Colombia, Jordan, Qatar, Singapore, South Korea, Thailand, Turkey and United Arab Emirates. VYZULTA is indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

- Our partnership with Samil Pharmaceutical concerning **ZERVIATE** in South Korea has been expanded to include Vietnam.

- Our Chinese partner Ocumension Therapeutics successfully completed a Phase 3 clinical trial of **ZERVIATE** (cetirizine ophthalmic solution), 0.24% in Chinese patients with allergic conjunctivitis in which ZERVIATE was compared to emedastine difumarate ophthalmic solution, 0.05%, an antihistamine marketed under the brand name EMADINE®. ZERVIATE was found to be non-inferior to emedastine difumarate in the primary efficacy endpoint of change from baseline in the itching score in the 24 hours prior to the Day 14 visit. ZERVIATE was safe and well-tolerated with no difference in the proportion of patients with adverse events compared to emedastine difumarate. This Phase 3 clinical trial was required for Ocumension to be able to submit a New Drug Application (NDA) for approval to commercialize ZERVIATE in China.

[1] Bloomberg data, comparing the period of the weeks ending 7 January 2022 to 1 April 2022 with the period of the weeks ending 8 January 2021 to 2 April 2021

Other partnerships

- The U.S. FDA has granted Orphan Drug Designation for **naproxcinod** for the treatment of sickle cell disease, which affects an estimated 100,000 Americans. Naproxcinod is a nitric oxide (NO)-donating naproxen combining the cyclooxygenase (COX) inhibitory activity of naproxen with that of nitric oxide developed by Nicox and exclusively licensed to Fera in the U.S. Nicox has tested naproxcinod in over 2,700 patients in osteoarthritis, generating a significant package of clinical safety data which is available to support Fera's development of naproxcinod, and ultimately an NDA submission for sickle cell disease.

Management and Advisors

In December 2021, we announced the appointment of Doug Hubatsch as Chief Scientific Officer to lead all of the Company's non-clinical and clinical development activities. Based in Nicox's U.S. subsidiary Nicox Ophthalmics Inc., he is responsible for setting the research and development strategy of the Group and is a member of the Nicox Executive Committee.

In July 2021, we announced that two internationally recognized experts in glaucoma, Robert N. Weinreb, M.D., Distinguished Professor and Chair, Ophthalmology and Director, Shiley Eye Institute, University of California San Diego, and Sanjay G. Asrani, M.D., Professor of Ophthalmology, Duke University, joined the Nicox Glaucoma Clinical Advisory Board.

2021 Financial Summary

Net revenue[2] for the full year 2021 was €7.2 million (€2.4 million in net royalties, €4.8 million in license payments), compared to €12.9 million (€2.4 million in net royalties, €10.5 million in license payments) for the full year 2020. The principal difference in revenue is due to an IFRS treatment of a licensing payment received from our partner Ocumension Therapeutics in 2020.

Operating expenses for the year 2021 increased to €25.1 million from €19.5 million for the previous year among which €5.2 million comes from non-clinical and development expenses due to the advancement and progress of the Phase 3 trials on NCX 470.

Net loss of the Nicox Group for the full year 2021 was €43.8 million against €18.1 million for the full year 2020. However, the 2021 net loss includes €27.8 million of non-recurring, non-cash items due to a reduction in the estimated fair value of ZERVIATE (of €12.7 million) and of NCX 4251 (of €15.1 million) reflecting, respectively, the changes in the allergic conjunctivitis market in the U.S. and the changes in the development plan and timeline for NCX 4251.

As of December 31, 2021, the Nicox Group had cash and cash equivalents of €42.0 million, as compared with €47.2 million at December 31, 2020, and as previously announced, the Company is financed until Q4 2023, assuming the development of NCX 470 alone.

As of December 31, 2021, the Nicox Group had financial debt of €20.5 million, consisting of €18.5 million in the form of a bond financing agreement with Kreos Capital signed in January 2019 and a €2 million credit agreement guaranteed by the French State, and granted in August 2020 in the context of the COVID-19 pandemic.

First Quarter 2022 Financial Highlights

As of March 31, 2022, the Nicox Group had cash and cash equivalents of €35.1 million as compared with €42.0 million at December 31, 2021. Net revenue[2] for the first quarter of 2022 was €0.7 million (entirely composed of net royalty payments). Net revenue[2] for the first quarter of 2021 was €1.7 million (including €0.7 million of net royalty payments).

[2] Net revenue consists of revenue from collaborations less royalty payments which corresponds to Net profit in the consolidated statements of profit or loss

As of March 31, 2022, the Nicox Group had financial debt of €20.5 million consisting of €18.5 million in the form of a bond financing agreement with Kreos Capital signed in January 2019 and a €2 million credit agreement guaranteed by the French State, and granted in August 2020 in the context of the COVID-19 pandemic.

Only the figures related to the cash position, revenue and debt of the Nicox Group as of December 31, 2021 and December 31, 2020 are audited; all other figures of this press release are non-audited.

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 nitric oxide-donating prostaglandin analog, for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The Company is also developing NCX 4251, a proprietary formulation of fluticasone, for dry eye disease. 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 Southeast Asian markets.

Nicox is headquartered in Sophia Antipolis, France, is listed on Euronext Paris (Compartment C: 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	Dylan van Haaften	Paris, France
Edison Investment Research	Pooya Hemami	London, UK
H.C. Wainwright & Co	Yi Chen	New York, U.S.
Kepler Cheuvreux	Damien Choplain	Paris, France

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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.

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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 3rd chapter of the '*Document d'enregistrement universel, rapport financier annuel et rapport de gestion 2020*' filed with the French *Autorité des Marchés Financiers* (AMF) on March 1, 2021 and in the 2nd chapter of the amendment to the "*Document d'Enregistrement Universel, rapport financier annuel et rapport de gestion 2020*" filed with the AMF on December 9, 2021 which are available on Nicox's website (www.nicox.com).

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CONSOLIDATED STATEMENTS OF PROFIT OR LOSS (DRAFT)

	As of December 31:	
	2021	**2020**
Revenue from collaborations	**8,583**	**14,423**
Royalty payments	(1,350)	(1,516)
Net profit	**7,233**	**12,907**
Research and development expenditures	(17,910)	(12,728)
Administrative expenses	(7,000)	(6,677)
Other income	843	1,083
Other expenses	(211)	(93)
Operating loss before amortization and impairment of intangible assets	**(17,045)**	**(5,508)**
Amortization of intangible assets	(1,205)	(1,252)
Impairment of intangible assets (1)	(27,760)	-
Operating loss	**(46,010)**	**(6,760)**
Finance income	3,456	1,168
Finance expense (2)	(4,851)	(12,478)
Net financial income, (expense)	**(1,395)**	**(11,310)**
Loss before tax	**(47,405)**	**(18,070)**
Income tax (expense) / benefit	3,644	(28)
Loss after tax	(43,761)	(18,098)
Loss for the period	**(43,761)**	**(18,098)**

(1) Includes two non–cash adjustments on US ZERVIATE estimated fair value decreasing by €(12.7) million, due to changes in the United States allergic conjunctivitis market, and on NCX 4251 estimated fair value, decreasing by €(15.1) million, reflecting the changes made to the development plan and timeline for NCX 4251.

(2) Includes in 2021 a net loss of €(3.3) millions related to the restructuration of the Kreos debt and in 2020 a net loss of €(6.9) millions following the divestment of VISUfarma shareholding and loan.

CONSOLIDATED STATEMENTS OF FINANCIAL POSITION (DRAFT)

	As of December 31:	
	2021	2020
ASSETS		
Non-current assets		
Goodwill	25,637	23,663
Intangible assets	39,974	64,848
Property, plant and equipment	1,023	1,166
Non-Current financial assets	237	68
Total non-current assets	**66,871**	**89,745**
Current assets		
Trade receivables	1,086	1,723
Government grants receivables	1,452	736
Other current assets	377	237
Prepayments	2,853	2,630
Cash and cash equivalents	41,970	47,195
Total current assets	**47,738**	**52,521**
TOTAL ASSETS	**114,609**	**142,266**
EQUITY AND LIABILITIES		
Shareholders' equity		
Issued capital	43,138	37,030
Share premium	536,200	528,595
Cumulative translation adjustement	5,953	2,959
Treasury Shares	(847)	(605)
Accumulated deficit	(508,892)	(467,144)
Total equity	**75,552**	**100,835**
Non-current liabilities		
Non-current financial liabilities	21,160	13,429
Deferred taxes liabilities	9,236	11,868
Provisions	661	730
Total non-current liabilities	**31,057**	**26,027**
Current liabilities		
Current financial liabilities [3]	346	5,646
Trade payables	3,649	2,421
Deferred income	1,970	5,174
Other current liabilities	2,035	2,163
Total current liabilities	**8,000**	**15,404**
TOTAL LIABILITIES AND EQUITY	**114,609**	**142,266**