

## Press Release

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# Nicox's Partner Fera Pharmaceuticals to Investigate Naproxcinod as Potential Covid-19 Adjuvant Treatment

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December 11, 2020 – release at 7:30 am CET  
Sophia Antipolis, France

**Nicox SA** (Euronext Paris: FR0013018124, COX), an international ophthalmology company, and Fera Pharmaceuticals, a privately-held, U.S. specialty pharmaceutical company, announced today that Fera will evaluate naproxcinod as a potential adjuvant treatment for patients with COVID-19 infection. Subject to successful completion of the ongoing manufacturing of naproxcinod test material, Fera plans to initiate pre-clinical proof-of-concept studies in models of COVID-19 infection in early 2021.

Naproxcinod, a Cyclooxygenase-Inhibiting Nitric Oxide (NO)-Donating (CINOD) naproxen, is a non-steroidal anti-inflammatory product candidate engineered to release NO and naproxen, originally discovered and developed by Nicox. Nicox and Fera entered into an agreement in December 2015 which granted Fera exclusive rights to develop and commercialize naproxcinod for the U.S. market. Nicox and Fera are amending their existing agreement to include COVID-19 as an indication, and Nicox will grant to Fera warrants<sup>1</sup> to acquire 10,000 Nicox shares.

**Michele Garufi, Chief Executive Officer and Chairman of Nicox**, said: *“There is a strong scientific rationale for using naproxcinod in the treatment of the inflammatory symptoms of COVID-19 infections, and potentially against the virus itself. In collaboration with Fera we will be testing this scientific rationale in relevant pre-clinical models and whilst this research is at an early stage, any potential future human trial would benefit from the extensive naproxcinod clinical data previously generated by Nicox for the treatment of signs and symptoms of osteoarthritis.”*

### Rationale for naproxcinod in COVID-19 treatment

Most outcomes of COVID-19 are associated with high levels of inflammation and dysfunction of the vascular system leading to thrombotic events<sup>2</sup>. Naproxcinod, a Cox-Inhibiting Nitric Oxide Donor (CINOD), would potentially treat multiple aspects of COVID-19 infection including fever, pain, inflammation and platelet aggregation, thus decreasing the risk of thrombus formation. In addition, NO donation might increase vasodilation and restore normal vascular functions. Moreover, NO has specifically been demonstrated to inhibit replication of the COVID-19 virus by two distinct mechanisms<sup>3</sup>. As an oral capsule formulation, naproxcinod could be easily administered to patients at the first signs of infection.

Once Fera has received the newly manufactured naproxcinod, they plan to initiate proof-of-concept pre-clinical tests in models of COVID-19 infection. Should the results of these studies prove positive, Fera plans to meet with the U.S. Food and Drug Administration (FDA) to identify the clinical trials that would be required to submit a New Drug Application (NDA) for naproxcinod in the treatment of COVID-19 infection.

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<sup>1</sup> The warrants will be issued at no cost. The subscription price of the new shares to be obtained by exercising the warrants will be equal to the VWAP calculated on the 3-days trading prior to the Board meeting that will decide on the issuance of the warrants.

<sup>2</sup> Bickdeli et al., COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020; 75(23):2950-2973.

<sup>3</sup> S. Akerstrom et al., Dual effect of nitric oxide on SARS-CoV replication: Viral RNA production and palmitoylation of the S protein are affected. Journal of Virology 2009; 395:1-9.



Under the terms of the naproxinod agreement with Nicox, Fera is responsible for all clinical development, manufacturing, regulatory and commercialization activities in the U.S. Nicox retains all rights to naproxinod outside the U.S., subject to the payment of royalties to Fera, if intellectual property developed under the agreement is used outside the U.S.

Fera continues to review non-COVID-19 development options for naproxinod, including addressing the U.S. FDA refusal letter concerning Fera's application for Orphan Drug Designation (ODD) of naproxinod in sickle-cell disease.

#### About naproxinod

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Naproxinod is a nitric oxide (NO)-donating naproxen combining the cyclooxygenase (COX) inhibitory activity of naproxen with that of NO (COX-inhibiting NO donor, CINOD). While the inhibitory COX component provides the analgesic and anti-inflammatory efficacy, the NO part may play a significant role in maintaining vascular endothelial cell function and integrity, blood pressure homeostasis and microvascular circulation. A broad clinical package already exists for naproxinod in osteoarthritis, including three phase 3 trials with over 2,700 patients.

#### About Fera Pharmaceuticals

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Fera Pharmaceuticals is a privately held company. The company goal is to realize opportunities via acquisitions, in-licensing, developing and marketing abbreviated new drug applications (ANDAs), new drug applications (NDAs) and 505(b)(2) NDA products. Areas of interest include products that could benefit from lifecycle management with a special focus on niche markets. For more information visit [www.ferapharma.com](http://www.ferapharma.com).

#### About Nicox

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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 ZERVIAE™ 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](http://www.nicox.com).

#### Analyst coverage

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Bryan, Garnier & Co	Victor Floc'h	Paris, France
Cantor Fitzgerald	Louise Chen	New York, U.S.
H.C. Wainwright & Co	Yi Chen	New York, U.S.
Kepler Cheuvreux	Damien Choplain	Paris, France
Oppenheimer & Co	Hartaj Singh	New York, U.S.



*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.*

#### Contacts

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##### Nicox

Gavin Spencer  
Executive Vice President, Chief Business Officer  
& Head of Corporate Development  
T +33 (0)4 97 24 53 00  
[communications@nicox.com](mailto:communications@nicox.com)

Investors & Media  
United States & Europe  
LifeSci Advisors, LLC  
Mary-Ann Chang  
T +44 7483 284 853  
[mchang@lifesciadvisors.com](mailto:mchang@lifesciadvisors.com)

Media  
France  
LifeSci Advisors, LLC  
Sophie Baumont  
M +33 (0)6 27 74 74 49  
[sophie@lifesciadvisors.com](mailto:sophie@lifesciadvisors.com)

## Forward-Looking Statements

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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 (i) in the 3<sup>rd</sup> 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](http://www.nicox.com)) and (ii) as restated in the 4<sup>th</sup> chapter of the half yearly financial report as of June 30, 2020, which is also available on Nicox's website.

**Nicox S.A.**  
Drakkar 2  
Bât D, 2405 route des Dolines  
CS 10313, Sophia Antipolis  
06560 Valbonne, France  
T +33 (0)4 97 24 53 00  
F +33 (0)4 97 24 53 99