



Third pivotal phase 3 study for NicOx' naproxcinod shows positive efficacy, safety and blood pressure results

First CINOD meets all three co-primary endpoints ($p < 0.001$) in the 303 hip osteoarthritis (OA) study and shows no detrimental effect on blood pressure

November 24, 2008. Sophia Antipolis, France. www.nicox.com

NicOx S.A. (NYSE Euronext Paris: COX) today announced that the third pivotal phase 3 study for naproxcinod in patients with OA of the hip showed a highly statistically significant result ($p < 0.001$) on all three co-primary efficacy endpoints of the trial. Naproxcinod 750 mg bid showed the same gastrointestinal (GI) adverse event rate and a similar blood pressure profile to placebo. Naproxcinod is the most advanced compound in a novel class of anti-inflammatory agents known as Cyclooxygenase-Inhibiting Nitric Oxide Donators (CINODs).

Following the positive results from the 301 and 302 studies in patients with OA of the knee, 303 represents the third phase 3 study for naproxcinod to achieve $p < 0.001$ on all three co-primary efficacy endpoints. The 303 study is also the final pivotal trial that NicOx plans to include in the submission of a New Drug Application (NDA) to the US Food and Drug Administration (FDA) in mid-2009.

"This study has demonstrated clear-cut efficacy for naproxcinod 750 mg bid in hip OA, in addition to providing reassuring blood pressure and safety data," said Thomas J. Schnitzer, MD, PhD, Professor of Medicine at Northwestern University Feinberg School of Medicine, who advised NicOx on the design and analysis of the trial. "Meeting the primary endpoints of this study is a significant achievement, considering the difficulty in controlling the symptoms of hip OA patients. Few studies with other anti-inflammatory agents have focused only on people with hip OA, in part because of the increased difficulty in demonstrating efficacy in this population compared to knee OA. Additionally, the fact that the blood pressure data for naproxcinod and placebo were similar at all time points is also encouraging, as there is a definite need for new anti-inflammatory agents that do not increase blood pressure."

Results clearly support naproxcinod's non-detrimental blood pressure profile

The blood pressure data for naproxcinod 750 mg bid were consistent with those obtained in the 301 and 302 studies. Blood pressure was measured using standardized and controlled office blood pressure measurements (OBPM) at baseline and at weeks 2, 6 and 13 (see NOTE). At all time points, the patients treated with naproxcinod 750 mg bid showed a very similar blood pressure profile to those on placebo. In addition, naproxcinod 750 mg bid showed a clear reduction in systolic and diastolic blood pressure (SBP and DBP) compared to naproxen 500 mg bid at all time points. No stand alone statistical analysis of the blood pressure data from the 303 study was pre-specified.

As planned, NicOx will pool the blood pressure data from the three phase 3 studies (301, 302 and 303) according to a prospectively designed protocol that has been submitted to the FDA. The Company will disclose the top-line results of the pre-specified statistical analysis on the pooled data in the coming weeks.

Naproxcinod and placebo show the same gastrointestinal (GI) adverse event rate

Naproxcinod 750 mg bid showed good overall safety and tolerability. The percentage of patients who experienced one or more GI adverse events was the same for placebo and naproxcinod 750 mg bid at 15.5%, compared to 19.2% for naproxen 500 mg bid. In terms of the percentage of patients who experienced at least one adverse event overall, this was lower for naproxcinod 750 mg than naproxen 500 mg bid. There was not a single serious cardiovascular or serious GI adverse event in the naproxcinod arm during the 13 weeks of the 303 study, in contrast to the placebo and naproxen 500 mg bid arms.

Pascal Pfister MD, Chief Scientific Officer and Head of Research and Development at NicOx, commented: *“We believe these are extremely good results, with naproxinod demonstrating clear efficacy in this difficult type of osteoarthritis patients and showing the same GI adverse event rate as placebo. The blood pressure data are consistent with previous studies and we are keenly awaiting the important results of the pre-defined statistical analysis in the next few weeks, following the pooling of the 301, 302 and 303 blood pressure data. We are confident that these results will clearly demonstrate naproxinod’s non-detrimental blood pressure profile, in contrast to naproxen.”*

Design and results of the 303 study

The 303 study was a 13-week, double-blind, placebo and naproxen controlled trial in patients with OA of the hip. 810 patients were enrolled at 120 clinical centers in the United States, Canada and Europe. Eligible patients had a diagnosis of primary osteoarthritis of the hip of at least three months in duration and were randomized on a 2:2:1 basis to receive naproxinod 750 mg bid, placebo bid and naproxen 500 mg bid, respectively.

The three co-primary endpoints of the study compared the efficacy of naproxinod 750 mg bid to placebo, in terms of the mean change between baseline and week 13 in the following scores: the WOMAC™ pain subscale, the WOMAC™ function subscale and the subject’s overall rating of disease status. The results demonstrated that naproxinod was superior to placebo with high statistical significance ($p < 0.001$) on all three of these co-primary endpoints. These were the same endpoints as those used in the 301 and 302 phase 3 studies. No statistical comparison was made between naproxen 500 mg bid and the other two arms on the efficacy endpoints, due to the 2:2:1 randomization in the study, although numerical data show that naproxinod 750 mg bid behaved in a similar fashion to naproxen 500 mg bid on these efficacy scores. NicOx entered into a full-service agreement for the conduct of the 303 study with Covance Inc., a global contract research organization (CRO).

NOTE: Office Blood Pressure Measurements (OBPMs) were performed by a health care professional during a patient’s visit to the treatment center using a standard technique and equipment (i.e. a sphygmomanometer). OBPMs were performed in the morning and the time between intake of study-drug and measurement of OBPM was between 2 and 4 hours.

NicOx (Bloomberg: COX:FP, Reuters: NCOX.PA) is a product-driven biopharmaceutical company dedicated to the development and future commercialization of investigational drugs for unmet medical needs. NicOx is applying its proprietary nitric oxide-donating technology to develop an internal portfolio of New Chemical Entities (NCEs) in the therapeutic areas of inflammatory and cardio-metabolic disease.

Resources are focused on the development and pre-commercialization activities for naproxinod, a proprietary NCE and the first compound in the Cyclooxygenase-Inhibiting Nitric Oxide-Donating (CINOD) class of anti-inflammatory agents for the treatment of the signs and symptoms of osteoarthritis. Naproxinod has completed three pivotal phase 3 studies with positive results and the submission of a New Drug Application (NDA) to the US Food and Drug Administration (FDA) is projected for mid-2009.

Beyond naproxinod, NicOx has a pipeline containing multiple nitric oxide-donating NCEs, which are in development internally and with partners, including Pfizer Inc and Merck & Co., Inc., for the treatment of prevalent and underserved diseases, such as atherosclerosis, hypertension, widespread eye diseases and Chronic Obstructive Pulmonary Disease (COPD).

NicOx S.A. is headquartered in France and is listed on the NYSE Euronext Paris (Compartment B: Mid Caps).



This press release contains certain forward-looking statements. Although the Company believes its expectations are based on reasonable assumptions, these forward-looking statements are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated in the forward-looking statements.

For a discussion of risks and uncertainties which could cause actual results, financial condition, performance or achievements of NicOx S.A. to differ from those contained in the forward-looking statements, please refer to the Risk Factors ("Facteurs de Risque") section of the Document de Reference filed with the AMF, which is available on the AMF website (<http://www.amf-france.org>) or on NicOx S.A.'s website (<http://www.nicox.com>).

NicOx S.A.,
Les Taissounières – Bât HB4 – 1681 route des Dolines - BP313, 06906 Sophia Antipolis cedex, France. Tel. +33 (0)4 97 24 53 00 • Fax +33 (0)4 97 24 53 99

CONTACTS: <http://www.nicox.com>

NicOx: Karl Hanks Director of Investor Relations and Corporate Communication
Tel +33 (0)4 97 24 53 42 • hanks@nicox.com

Media in the United States – FD Robert Stanislaro • Tel +1 212 850 5657 • robert.stanislaro@fd.com
Irma Gomez-Dib • Tel +1 212 850 5761 • irma.gomez-dib@fd.com

Media in Europe – Citigate Dewe Rogerson David Dible • Tel +44 (0)207 282 2949 •
david.dible@citigatedr.co.uk

Nina Enegren • Tel +44 (0)207 282 1050 • nina.enegren@citigatedr.co.uk