Nicox submits New Drug Application for AC-170 to U.S. FDA

Dossier submitted, with a request for Priority Review, for the treatment of ocular itching associated with allergic conjunctivitis

April 19, 2016

Sophia Antipolis, France

Nicox S.A. (Euronext Paris: FR0013018124, COX), the international ophthalmic company, today announced the submission, through its American subsidiary Nicox Ophthalmics, Inc., of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for approval of AC-170, its novel, proprietary, cetirizine eye drop formulation, for the treatment of ocular itching associated with allergic conjunctivitis. Based on clinical pediatric data generated with AC-170, the Company also requested a Priority Review, which, if obtained, could result in an FDA decision by the end of 2016 based on PDUFA (Prescription Drug User Fee Act) performance goals.

Michele Garufi, Chairman and Chief Executive Officer of Nicox, stated. *"The submission of the first U.S. NDA resulting from our acquisition of Aciex in October 2014 is a major milestone in the Company's history and a significant step forward in our commitment to delivering new ophthalmology treatment options to patients. If successful in obtaining Priority Review, we would have two compounds – AC-170 and latanoprostene bunod, licensed to Bauch+Lomb, – potentially receiving FDA approval in the United States by the end of 2016. This would be a remarkable achievement for Nicox, and almost unique in the panorama of European biotech companies."*

"AC-170 is the first ocular product which utilizes the well-known antihistamine cetirizine," **commented Mike Bergamini, Chief Scientific Officer and Executive Vice President of Nicox**. *"The established safety and efficacy of this molecule, administered orally, is widely recognized by physicians, and our goal is for AC-170 to become a trusted medicine for the estimated 75 million Americans who currently suffer from allergic conjunctivitis."*

The FDA has a 60-day filing review period to determine whether the NDA is complete and acceptable for filing, and to confirm if the Priority Review has been granted. Nicox expects to communicate the Agency's decision.

About AC-170

AC-170 is a novel formulation of cetirizine, the active ingredient in Zyrtec®[1], which has been developed for the first time for topical application in the eye for the treatment of ocular itching associated with allergic

conjunctivitis. Cetirizine is a second generation antihistamine and mast cell stabilizer that binds competitively to histamine receptor sites to reduce swelling, itching and vasodilation. Cetirizine, as an approved oral drug, has a well-characterized systemic safety and efficacy profile with worldwide exposure representing more than 300 million patient-years[2-3-4]. AC-170 is covered by two granted U.S. patents expiring in 2030 and 2032.

Two Phase 3 safety and efficacy trials have been completed using the conjunctival allergen challenge (CAC) model of allergic conjunctivitis. Both Phase 3 clinical trials demonstrated statistically significant results for AC-170 compared to vehicle control (placebo) for the primary endpoint of ocular itching. Treatment emergent adverse events were similar in severity and frequency within the active and placebo groups.

Nicox held two pre-NDA meetings with the FDA regarding AC-170 for both its clinical development program and its chemistry, manufacturing, and controls aspects, respectively and the FDA recommended submission of the NDA.

Nicox is seeking regulatory approval for AC-170 utilizing the FDA's Section 505(b)(2) regulatory pathway, which enables the Company to rely, in part, on the FDA's prior findings of safety and efficacy for cetirizine and on the published literature, in support of the NDA. Approval of the AC-170 NDA prior to 1st December 2016 will trigger a milestone payment of $35 million in Nicox shares to ex-Aciex shareholders or $10 million in Nicox shares if approval of the NDA is received after this date. AC-170 was developed by Aciex Therapeutics, Inc., which became a wholly-owned subsidiary of Nicox in October 2014 and was subsequently renamed Nicox Ophthalmics, Inc.

In order to further support the clinical safety database, we have also commenced an additional clinical safety study on AC-170.

About allergic conjunctivitis

Allergic conjunctivitis occurs when an allergic reaction causes conjunctivitis. Conjunctivitis is an inflammation of the thin layer of tissue that lines the white surface of the eye and the inner surface of the eyelids. It is a common eye disease, especially in children, and may affect one or both eyes. The signs and symptoms may include eye redness, excessive watering, itchy burning eyes, discharge, blurred vision and increased sensitivity to light. Conjunctivitis can be caused by a viral or bacterial infection, or can be the result of an allergic reaction.

It is estimated that more than 75 million people suffer from allergic conjunctivitis in the U.S.[5] and the prevalence ranges from 20% to 40%[6-7]. The annual U.S. market for the treatment of allergic conjunctivitis totals more than $800 million[8].

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References

1. Zyrtec® is a trademark of UCB Pharma SA or GlaxoSmithKline.
2. Zyrtec® (Cross-discipline team-leader review).
3. Charlesworth, E.N., et al., Effect of cetirizine on mast cell-mediator release and cellular traffic during the cutaneous late-phase reaction. J Allergy Clin Immunol, 1989. 83(5): p. 905-12.
4. Levi-Schaffer, F. and R. Eliashar, Mast cell stabilizing properties of antihistamines. J Invest Dermatol, 2009. 129(11): p. 2549-51.
5. Global Data : Allergic Conjunctivitis Market Analysis, September 2014.
6. Nathan RA, Meltzer EO, et al. Prevalence of allergic rhinitis in the United States. J Allergy Clin Immunol 1997; 99(6)2:S808-S814.
7. Singh K, et al. Epidemiology of ocular and nasal allergy in the United States, 1988-1994. Journal of Allergy and Clinical Immunology; 2010. 126: 778–783.
8. IMS April 2014.

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About Nicox

Nicox (Bloomberg: COX:FP, Reuters: NCOX.PA) is an international commercial-stage company focused on the ophthalmic market. With a heritage of innovative R&D, business development and marketing expertise, Nicox is building a diversified portfolio of ophthalmic products that can help people enhance their sight.

Nicox's advanced pipeline features latanoprostene bunod for the lowering of intra-ocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension, and for which a New Drug Application (NDA) was submitted to the FDA by the Company's licensee Bausch + Lomb. The Company's pipeline also features AC-170, for which the NDA was submitted to the FDA for the treatment of ocular itching associated with allergic conjunctivitis in April 2016, as well as two pre-MAA candidates in Europe: AzaSite® for bacterial conjunctivitis and BromSite™ for pain and inflammation after cataract surgery. Beyond these late-stage candidates, Nicox is developing a pipeline of next generation ophthalmology-focused candidates which utilize its proprietary nitric oxide (NO)-donating research platform. The Group has operations in Europe and the United States.

Nicox is listed on Euronext Paris (Category B: Mid Caps) and is part of the CAC Healthcare, CAC Pharma & Bio and Next 150 indexes. For more information on Nicox, its commercial products or pipeline, please visit www.nicox.com.

Analyst coverage

Bryan, Garnier & Co	Hugo Solvet	Paris, France
Invest Securities	Martial Descoutures	Paris, France
Gilbert Dupont	Damien Choplain	Paris, France

Upcoming 2016 events

Financial and business conferences

April 12-13	Needham Healthcare Conference	New York, US
May 10	Gilbert Dupont Forum Santé	Paris, France
May 19	European Mid Small Cap Forum	London, UK
May 17	SFAF Bio Day	Paris, France
June 6-9	BIO 2016	San Francisco, US
July 12-13	Cantor Fitzgerald's 2nd Annual Healthcare conference	New York, US

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