Updated and additional risk factors as of March 5, 2015

The Company undertook a review of the risks that might have a negative impact on its business, its financial situation, its performances or its ability to achieve its goals and considers that there are no significant risks other than those mentioned in Chapter 4 of the 2013 Reference Document, those outlined in the Half-Year Financial Report of June 30, 2014 and those included in Chapter 5 of the First Update of the 2013 Reference Document filed with the AMF on 30 September 2014, as completed and updated below.

Risks associated with cash use and potential future cash requirements

As of the date hereof, the cash of the Company was estimated at approximately €23 million. The Company anticipates important cash requirements given the current monthly rate of use and the financing needs related to the following projects:

- The submission of a New Drug Application (NDA) for AC-170 to the American Food and Drug Administration (FDA) by the subsidiary Aciex Therapeutics Inc., acquired in October 2014;
- The development program of Xailin Viral (antiviral eye drop based on Carragelose® acquired in September 2014); and
- The development program of ophthalmic therapeutics AzaSite® and BromSite™ in Europe, following the exclusive license agreement signed with InSite in February 2015.

On the date hereof, the cash of the Company will not be sufficient to finance operations of the Company over the next 12 months, given the current monthly rate of consumption and needs in connection with the projects presented. However, the Board considers that the reserved share capital increase which is currently implemented, for which the Company benefits from subscription undertakings representing a net amount of approximately €25 million, will enable the Company, subject to its effective settlement, to obtain the funds needed for business continuity for at least 12 months.

Since 2012, Nicox has acquired marketing rights of several ophthalmic products in the United States[1] and in the main European markets as well as two commercial subsidiaries in Europe: Nicox Farma Srl (ex-Eupharmed), acquired in December 2013, and Doliage, acquired in September 2014. This strategy enabled the generation of a growing turnover. The growth of the turnover is likely to continue in 2015 and should benefit from the marketing of new products. However, the Group estimates that the sales will not be sufficient to allow it to make a profit in the short term. Given the strong competition on the ophthalmic markets targeted by Nicox (see Section 4.1.2 of the 2013 Reference Document), there is no guarantee that Nicox will reach its sales goals and that the business activity will become profitable in Europe. If the sales proved to be significantly below forecasts, the Group could be led to the implementation of measures in order to safeguard its cash flow, in the form of a reduction of its sales force in one or several European countries or by ceasing direct business activities in the country/countries with the weakest performance.

Nicox could need to raise additional funds due to many factors, including the costs relating to the development or registration and commercial deployment of new products. Consequently, the Company could be led to find other sources of financing, either:

- through a capital increase;
- in the form of a loan; or
- by signing strategic partnership agreements designed to generate new revenue from the use of its licenses and patents or to share operating costs.

Nicox cannot guarantee that its future capital needs will be satisfied, nor that additional financing will be available on acceptable terms. The failure to achieve one or several of those measures could have a significant negative impact on the Company, its business, its financial situation and its performances, as well as its development and perspectives. In case of an inability of the Group to obtain the necessary funding, it could be forced to delay, reduce or delete the expenses relating to some commercialized products or some projects under development, to seek finance through collaboration arrangements, to grant licenses for development or commercialization of products it would have preferred to develop, or to commercialize itself, which would lead to a decrease in the value the Group could withdraw from those products. Moreover, if it is financed through a capital increase, the shareholders would be exposed to a risk of dilution of their interest.

Risks associated with Vesneo™ (latanoprostene bunod), developed with Bausch+Lomb

Vesneo™ (latanoprostene bunod, previously called BOL-303259-X, NCX 116 and PF-03187207) is a nitric oxide-donating prostaglandin F2-alpha analog developed for the potential treatment of glaucoma and ocular hypertension. Latanoprostene bunod was licensed in March 2010 to Bausch + Lomb, a subsidiary of Valeant group.

Following the positive results in phase 3, Bausch + Lomb plans on submitting an NDA in the United States in the second quarter of 2015 and to launch Vesneo™ in the United States in the second quarter of 2016, subject to the approval of the FDA.

Two studies were also initiated in Japan: JUPITER (phase 3) and KRONUS (phase 1). A study confirming its efficacy is expected to be requested for the registration of the medication in Japan.

The Company has identified the following specific risks regarding Vesneo™:

Risks associated with the registration of Vesneo™ in the United States

Nicox identified the following main risks relating to the registration of Vesneo™ in the United States:

- There is a risk Bausch + Lomb may not be able to file the NDA in the second quarter of 2015 as planned. In the event of a delayed filing, it would postpone the potential launch of Vesneo™, which could have a negative impact on the financial situation of Nicox.
- As for any registration application, there is a risk that the FDA refuses to approve Vesneo™, which could have a negative impact on the financial situation and the perspectives of Nicox.
- Bausch + Lomb may decide to stop the development of Vesneo™ and not to register the molecule in the United States. If Bausch + Lomb decides to terminate the agreement with Nicox or if Nicox is unable to develop the medication internally or find another partner, its development would have to be permanently discontinued, which could have a negative impact on the financial situation and the prospects of the Company.

[1] It is reminded that Nicox sold its commercial American subsidiary Nicox Inc. to Valeant in November 2014 (see September 17, 2014 Nicox press release).

Risks associated with co-promotion option of Vesneo™ in the United States

In August 2014, Nicox informed Bausch + Lomb of its decision to exercise its option to co-promote the products containing latanoprostene bunod in the United States, including Vesneo™. If Nicox had the intention to promote an ophthalmic product competing with a product of Bausch + Lomb in the United States, Nicox should inform them at least 12 months before the launch of the product and Bausch + Lomb would then have the right to terminate the co-promotion agreement. This could have a negative impact on the turnover of the Group.

It is specified that AC-170, a drug-candidate developed by Nicox for the potential treatment of ocular itching associated with allergic conjunctivitis, could be considered as competing with a product of Bausch + Lomb which commercializes antihistaminic eye drops. Therefore, Nicox would have to inform Bausch + Lomb at least 12 months before the planned launch of AC-170, and Bausch + Lomb would then have the right to terminate the co-promotion agreement regarding Vesneo™.

Risks associated with the market potential of Vesneo™ in the United States

Assuming that Vesneo™ is approved and marketed in the United States, Nicox would receive royalties on net sales from 6% to 11% from Bausch + Lomb after deduction of payments due to Pfizer. Royalties collected by Nicox would depend on the sales reported by Bausch + Lomb, which would depend on the commercial success of Vesneo™ in the United States. Nicox cannot guarantee such commercial success. Bausch + Lomb estimate that the sales of Vesneo™ could reach approximately $500 million in the United States and approximately $1 billion worldwide. However, there is a risk that Bausch + Lomb overestimated this commercial potential and the real sales figures turn out to be less than expected:

- The US regulatory authorities may impose restrictions on the use or sale of Vesneo™. Such restrictions could limit the potential market, delay the launch and/or reduce the volume of sales of the product and its profitability.
- The commercial success of Vesneo™ would depend on several factors (none of which can be guaranteed by the company), including:
    - The acquisition by Bausch + Lomb of a regulatory label including references allowing the differentiation of Vesneo™ from other medications for treatment of glaucoma and ocular hypertension;
    - The acquisition by Bausch + Lomb of reimbursement conditions that meet the current expectations and of a sale price enabling a profitable commercialization;
    - The maintenance and development of Bausch + Lomb commercial production capacity allowing sufficient flexible conditions for the orders;
    - The acceptance of Vesneo™ by the medical community; and, more broadly,
    - Its successful launch, sale and distribution.

Specific risks associated with AC-170

AC-170 is a new formulation of cetirizine developed for the potential treatment of ocular itching associated with allergic conjunctivitis. AC-170 was developed by Aciex Therapeutics, Inc., a subsidiary of Nicox since its acquisition in October 2014.

The Company has identified the main specific risks of AC-170 below. Furthermore, it is recalled that all “Risks associated with Nicox’s strategy and activity: the research, development and marketing of therapeutics and medical devices” apply to AC-170 (see section 4.1.6 of the Reference Document 2013).

Risks relating to the registration of AC-170 in the United States

In a pre-NDA meeting, on the basis of available efficacy and safety clinical data, the FDA recommended the submission of an NDA. However, there is still a risk that additional clinical data would be necessary to obtain product approval, including in order to answer any questions the FDA might ask during the regulatory review process. Moreover, in the event that the FDA approves AC-170, there is no guarantee that the existing clinical data will be sufficient to obtain a favorable regulatory label, particularly in the instructions or the dosage, allowing a favourable positioning of the product among healthcare practitioners.

Therefore, there is a risk that Nicox may be required to conduct one or several additional clinical studies in order to strengthen the clinical dossier of AC-170 to aid the approval of the medication and/or to enhance the regulatory label. This could cause extra development costs for the Group and delays in the approval and the launch of the product.

Like for any registration application, there is a risk that the FDA refuses to approve the product, which could have a negative impact on the financial situation and the prospects of the Group.

Risks associated with the launch of AC-170 in case of potential approval

To date, Nicox does not have any commercial infrastructure in the United States. It should be recalled that Nicox had a commercial infrastructure specialising in diagnostic tests until November 2014, on which date its subsidiary Nicox Inc. was acquired by Valeant.

If AC-170 were to be approved in the United States, Nicox should consider several options to place this medication on the market:

- Nicox could create a new American commercial infrastructure to directly promote AC-170. This would generate important costs and there is no guarantee that the sales of AC-170 would be sufficient to cover the cost of such infrastructure. The profitability of this possible infrastructure could depend on the product portfolio of the Group when implemented. In addition, Nicox might not be able to establish an adequate structure to ensure the commercial success of AC-170, which could have a negative impact on the commercial potential of this medication and on its valuation in the portfolio of the Group.
- Nicox could conclude one or several sales, license or distributions agreements with third parties. However, the Group might not be able to conclude any agreements under acceptable terms or may not be able to conclude any agreement whatsoever. If the Group decided to conclude such agreements with third parties, its potential income would depend on the terms of the agreements and the performances of those companies in promoting and selling.

Risks associated with the market potential of AC-170 in the United States

Even supposing that AC-170 was approved by the FDA and then launched in the United States, the Company cannot ensure that it will bring any commercial success:

- Regulatory authorities could impose restrictions on the use or sale of AC-170 which may limit the potential market, delay the launch and/or reduce the level of sales and the profitability of the product;
- The commercial success of AC-170 will depend on a number of factors (none of which can be guaranteed by the Company), amongst others:

- The obtaining by Nicox of reimbursement with respect to the product conforming to current expectations and of a sale price enabling a profitable commercialization;
- The maintenance and development of commercial production capacity allowing sufficient flexible conditions for the orders;
- The acceptance of AC-170 by the healthcare community; and, more broadly,
- The success of the launch, commercial sales and distribution.

Specific risks associated with AzaSite and BromSite, in-licensed from InSite Vision

AzaSite® and BromSite™ are two drug-candidates in-licensed from InSite Vision in February 2015 for Europe, Middle East and Africa. AzaSite® targets the treatment of bacterial conjunctivitis. BromSite™ targets the treatment of inflammation and prevention of pain after cataract surgery. Nicox plans on submitting European Marketing Authorisation Applications (MAAs) for those two products by the first quarter of 2016, the first commercial launch being expected by the end of 2017.

The Company has identified the main specific risks relating to AzaSite® and BromSite™ below. Furthermore, it is recalled that all "Risks associated with Nicox's strategy and activity: The research, development and marketing of therapeutics and medical devices" must apply to AzaSite® and BromSite™ (see section 4.1.6 of the Reference Document 2013).

Risks associated with the registration of AzaSite® and BromSite™ in Europe

There is a risk that Nicox may not submit one and/or another of the two MAAs by the first quarter of 2016. As a matter of fact, resources dedicated to development and regulatory matters are limited and there is no guarantee that they will be sufficient for the submission of one or both MAAs within the expected time limits. If Nicox were to delay the filing date of the dossier for AzaSite® and/or BromSite™, it would postpone the launch of this/those candidates on the market, which could have a negative impact on the financial situation of the Group.

Furthermore, regarding the submission of the MAA of AzaSite® and BromSite™, Nicox will have the right to use the data from the American registration dossier of AzaSite®, which is already approved in the United States, and the data obtained in the studies undertaken with BromSite™. If Nicox estimates that no additional clinical study should be required before the inclusion of authorisation dossiers, the possibility cannot be excluded that extra clinical data will be necessary to obtain the approval of either product, including answering the questions the European regulatory agencies might ask during the review process. Moreover, there is no guarantee that the existing clinical data will permit to obtain a favourable regulatory label allowing them to be distinguished from existing competing medications.

Therefore, there is a risk that Nicox will be obliged to carry out one or several additional clinical studies in order to reinforce the clinical dossier of AzaSite and/or BromSite to promote their approval and/or to enhance the regulatory label. This could cause additional development costs for the Group and delays in the approval and launch of the product.

Like for any other registration application, there is a risk the European authorities will refuse to approve AzaSite® and/or BromSite™, which could have a negative impact on the financial situation of the Group.

Risks associated with the commercial potential of AzaSite® and BromSite™ in case of potential approval

If AzaSite® and/or BromSite™ are approved in Europe, they would be in competition with many other medicines already available in their respective indications. Their commercial success would depend on several factors (none of which may be guaranteed by the Company), amongst others:

- The skill of the sales team of Nicox or its distributors, according to the territory;
- The price and reimbursement terms;
- The maintenance and development of commercial operating capacities with third parties;
- The acceptance of the medication by the healthcare community; and
- The availability of the medication in pharmacies.