NOXXON PUBLISHES PRECLINICAL PROOF-OF-CONCEPT DATA FOR LEAD COMPOUND NOX-A12 IN COMBINATION WITH CHECKPOINT INHIBITORS

New preclinical data in *Cancer Immunology Research* demonstrate that increasing tumor-infiltrating T cells through inhibition of CXCL12 by NOX-A12 synergizes with PD-1 checkpoint inhibition

Berlin, Germany, October 03, 2017 - NOXXON Pharma N.V. (EuroNext Growth Paris: ALNOX), a biotechnology company focused on improving cancer treatments by targeting the tumor microenvironment (TME), announced today the publication of novel preclinical data for NOXXON's lead cancer compound, NOX-A12 (olaptesed pegol). The results highlighted the effects of NOX-A12 *in vitro* and in an animal model, emphasizing NOX-A12's ability to enhance the infiltration of T and NK immune cells into tumor tissue thereby synergizing with and overcoming resistance to PD-1 checkpoint inhibition with the goal of enabling the destruction of cancer. Building on extensive clinical experience and safety data, the lead program NOX-A12 will deliver top-line data from a Keytruda® combination trial in metastatic colorectal and pancreatic cancer patients in 2018.

"Immune checkpoint inhibitors promote T cell-mediated killing of cancer cells and induce striking responses. However, as only a subset of patients benefits from such treatment, novel strategies to enhance the effect are needed. Although preclinical, we believe that the results of this study further validate the potential of NOX-A12 as a combination therapy to improve outcomes in multiple oncology indications," said Aram Mangasarian, CEO of NOXXON. "The goal of our current clinical trial is to reproduce these results and to deliver a meaningful therapeutic impact in colorectal and pancreatic cancer patients."

The pre-clinical study titled "Increasing tumor-infiltrating T cells through inhibition of CXCL12 with NOX-A12 synergizes with PD-1 blockade" aimed to evaluate the potential of NOX-A12 as a combination therapy approach to improve checkpoint inhibition therapies. In particular, the study investigated whether NOX-A12-based inhibition of the chemokine CXCL12, a key factor in TME-driven immune suppression, would increase lymphocyte infiltration into the tumor and thus enable effective killing of cancer cells in combination with checkpoint inhibitors. By employing three-dimensional cell culture models that mimic a solid tumor with a CXCL12-abundant TME, it was demonstrated that NOX-A12 enhanced the infiltration of T and NK cells in a dose-dependent manner. NOX-A12 and PD-1 checkpoint inhibition synergistically enhanced T cell activation in the model indicating that both agents complement each other. The findings were subsequently validated *in vivo* in a murine model of colorectal cancer where the addition of NOX-A12 significantly improved anti-PD-1 therapy. Taken together, the results demonstrate that CXCL12 inhibition can break the immune-privilege of the TME by paving the way for immune effector cells into the tumor and that NOX-A12 could be an important therapeutic approach to broadening the applicability of checkpoint inhibitors in cancer patients.

The results, published in the current issue of *Cancer Immunology Research* can be accessed through the current online version of the journal and the following link:
http://cancerimmunolres.aacrjournals.org/cgi/content/abstract/2326-6066.CIR-16-0303

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About NOXXON

NOXXON's oncology-focused pipeline acts on the cancer immunity cycle by breaking the tumor protection barrier, blocking tumor repair and exposing hidden tumor cells. Through neutralizing chemokines in the tumor microenvironment, NOXXON's approach works in combination with other forms of treatment to weaken tumor defenses against the immune system and enable greater therapeutic impact. Building on extensive clinical experience and safety data, the lead program NOX-A12 will deliver top-line data from a Keytruda® combination trial in metastatic colorectal and pancreatic cancer patients in 2018. Further information can be found at: www.noxxon.com

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