

CORRECTED PRESS RELEASE¹: NOXXON ANNOUNCES POSITIVE RESULTS FROM SECOND COHORT IN PHASE 1/2 NOX-A12 BRAIN CANCER TRIAL

This press release corrects a prior version published on June 1, 2021 and is updated to include maximal tumor reductions from baseline in the 2nd cohort. The corrected press release reads:

Berlin, Germany, June 8, 2021, 08:00 a.m. CEST - NOXXON Pharma N.V. (Euronext Growth Paris: ALNOX), a biotechnology company focused on improving cancer treatments by targeting the tumor microenvironment (TME), announced today positive results from the second cohort in its Phase 1/2 study of NOX-A12 in combination with radiotherapy in patients with brain cancer (Glioblastoma Multiforme). Data show that NOX-A12 at 400mg/week continues to be safe and well tolerated with apparent signals of reduction of tumor size.

The study investigates three dose regimens of NOX-A12 (200, 400 and 600 mg/week), each combined with external-beam radiotherapy in newly diagnosed brain cancer patients. The six patients in the first two cohorts (3 patients receiving 200 mg/week and 3 patients receiving 400 mg/week) have now completed NOX-A12 therapy, with over 83% of these patients showing reductions in tumor size during or after NOX-A12 treatment with maximal reductions from baseline ranging from 2% to 62%² for patients treated at 200 mg/week (1st cohort), and 28% and 71%^{1,2} for two patients treated at 400 mg/week (2nd cohort). These patients tolerated combined radiotherapy and NOX-A12 therapy well without any signs of dose-limiting toxicities.

Two patients, one in each of the first two cohorts, achieved objective responses with tumor reductions greater than 50%, one of which occurred after cessation of NOX-A12 therapy. In three of the six patients, smaller satellite lesions that were present before therapy around the primary tumor completely disappeared. In cohort 1 (200mg/week), two of three patients have survived past the expected average survival of 10 months. Further analysis of survival in each cohort is still pending follow-up.

"These exciting clinical data show a substantial impact on tumor size following treatment with NOX-A12, which continues to be safe and well tolerated in this challenging patient population. We are looking forward to continuing this study and generating further data on the potential of NOX-A12 to make a significant difference to patients in urgent need of effective and safe treatment. Enrolment of patients in the third cohort has been completed and we expect results from the last cohort in Q4 2021," **commented Aram Mangasarian, CEO of NOXXON.**

NOX-A12 targets CXCL12 (C-X-C Chemokine Ligand 12), a key chemokine protein that communicates between tumor cells and their environment, and is designed to 1) block repair of destroyed blood vessels and 2) break tumor protection against the immune system, enabling anti-cancer immune cells, such as killer T-cells, to enter tumor tissue and attack the cancer cells.

¹ Press release issued on June 1, 2021 specified the maximal tumor reductions from baseline in the 1st cohort treated with NOX-A12 at a dose of 200 mg/week but omitted to mention the maximal tumor reductions from baseline in the 2nd cohort treated with NOX-A12 at a dose of 400 mg/week

² SPD assessed by MRI using a central reader.

Advanced MRI imaging techniques showed that five of six patients in the first two cohorts achieved reduced blood flow to the tumor compared with baseline³, suggesting that NOX-A12 combined with radiotherapy was able to prevent blood vessel regrowth, a key mechanism of action predicted by preclinical data. The pharmacologic effect was further supported by comparison of pre-treatment to on-therapy tumor tissue from one patient in cohort 1, revealing a disappearance of CXCL12 from the barrier cells that separate the blood from the tissue, suggesting that NOX-A12 was able to effectively suppress its target⁴.

This tissue comparison also showed an extensive reduction in the number of actively dividing tumor cells, reaching almost zero in the on-therapy sample, and clusters of expanding cytotoxic immune cells throughout the under-treatment sample. This supports the notion that NOX-A12 can facilitate an entrance of immune cells into the tumor and an anti-tumoral immune response⁵, already at the lowest tested dose in the study.

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About NOXXON

NOXXON's oncology-focused pipeline acts on the tumor microenvironment (TME) and the cancer immunity cycle by breaking the tumor protection barrier and blocking tumor repair. By neutralizing chemokines in the TME, NOXXON's approach works in combination with other forms of treatment to weaken tumor defenses against the immune system and enable greater therapeutic impact. NOXXON's lead program NOX-A12 has delivered final top-line data from a Keytruda® combination trial in metastatic colorectal and pancreatic cancer patients published at the ESMO conference in September 2020 and based on the trial results, including overall survival and safety profile, further studies are being planned in pancreatic cancer. NOXXON is also studying NOX-A12 in brain cancer in combination with radiotherapy which has been granted orphan drug status in the US and EU for the treatment of certain brain cancers. A trial of NOX-A12 in combination with radiotherapy in newly diagnosed brain cancer patients who will not benefit from standard chemotherapy has delivered interim data from the first two cohorts showing consistent tumor reductions. The company's second clinical-stage asset NOX-E36 is a Phase 2 TME asset targeting the innate immune system. NOXXON plans to test NOX-E36 in patients with solid tumors. Further information can be found at: www.noxxon.com

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³ rCBV assessed by MRI using a central reader

⁴ Assessed by multiplexed immunofluorescence microscopy (CODEX®)

⁵ Assessed by CODEX® using Ki67 and cytotoxic immune cell markers



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