

**PRESS RELEASE**



**NOXXON Initiates Phase IIa Trial of anti-CXCL12/SDF-1 Spiegelmer®  
NOX-A12 in Second Oncology Indication: Multiple Myeloma**

**Berlin, Germany- 26 September 2012-** NOXXON Pharma today announced the treatment of the first cohort of three multiple myeloma (MM) patients in a Phase IIa clinical trial of its anti-CXCL12/SDF-1 (CXC chemokine ligand 12 / Stromal Cell-Derived Factor-1) Spiegelmer® NOX-A12. CXCL12 signaling has been shown to play an important role in the pathophysiology of MM, especially in the interaction of MM cells with the bone marrow microenvironment. By inhibiting this interaction NOX-A12 sensitizes the cancer cells to chemotherapy.

This is the third Phase IIa trial that NOXXON has started this year following the NOX-E36 Phase IIa for the treatment of diabetic nephropathy in June and the NOX-A12 Phase IIa for the treatment of Chronic Lymphocytic Leukemia in July.

MM is a hematologic or blood cancer that develops in the bone marrow in which normal antibody-producing cells transform into malignant myeloma. The growth of the cancer cells in the bone marrow blocks production of normal blood cells and antibodies, and also causes lesions that weaken the bone. According to the US National Cancer Institute (NCI), MM is the second most common blood cancer in the United States and accounts for approximately one percent of all cancers.

NOXXON's multi-center, open-label, uncontrolled study will be conducted in Europe on 28 relapsed MM patients who were all previously treated for their cancer. The patients will receive NOX-A12 in combination with a background therapy of Velcade®/bortezomib and dexamethasone (VD). Combination treatment with NOX-A12 and VD will occur in 8 cycles of 21 days, with a follow-up period of one year. Each patient will receive up to three different doses of NOX-A12 as part of an individualized dose titration. The primary efficacy endpoint of the study will be the overall response rate, which includes patients with complete and partial responses to therapy. NOXXON expects interim results to be available by the end of 2012.

Although VD is one of the established therapies for MM, there remains significant need for improved therapy in relapsed patients. Recent publications indicate that the complete response rate for VD therapy of relapsed/refractory MM is approximately 17%<sup>1</sup>.

NOX-A12 is the only anti-cancer agent in active clinical development that neutralizes CXCL12, thereby resulting in a complete block of CXCL12 signaling through its two receptors, CXCR4 and CXCR7. Competing agents currently in clinical trials act at the receptor level and only inhibit CXCR4.

Based on information from the NCI, the American Cancer Society and the GLOBOCAN database, NOXXON estimates that there are approximately 100,000 MM patients requiring treatment every year in the combined markets of the EU-5 (France, Germany, Italy, Spain and the United Kingdom), Japan and the United States.

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**Notes for editors:**

**About NOXXON Pharma AG**

NOXXON Pharma is a biopharmaceutical company pioneering the development of a new class of proprietary therapeutics called Spiegelmers. Spiegelmers are the chemically synthesized, non-immunogenic alternative to antibodies. NOXXON has a diversified portfolio of clinical-stage Spiegelmer® therapeutics:

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<sup>1</sup> Corso A, Eur J of Haematol. 2009, 83 (449–454) ; Dimopoulos MA, International Myeloma Foundation, 2010 ; Igarashi N, Int J Hematol 2010, 92:518–523 & Kobayashi T, Int J Hematol. 2010 Nov;92(4):579-8

- NOX-E36 is an anti-CCL2/MCP-1 (C-C chemokine ligand 2 / Monocyte Chemoattractant Protein-1) Spiegelmer<sup>®</sup> currently in a Phase IIa study in patients with type 2 diabetes with albuminuria. CCL2 is a pro-inflammatory chemokine involved in recruitment of immune cells to inflamed tissues.
- NOX-A12 is an anti-CXCL12/SDF-1 (CXC chemokine ligand 12 / Stromal Cell-Derived Factor-1) Spiegelmer<sup>®</sup> that is currently in Phase IIa studies in two hematological cancers, multiple myeloma (MM) and chronic lymphocytic leukemia (CLL). CXCL12 is a chemokine mediator of tumor invasion, metastasis, and resistance to chemotherapy.
- NOX-H94 is an anti-hepcidin Spiegelmer<sup>®</sup> that has completed a comprehensive single and multiple ascending dose Phase I study and a Phase I endotoxin challenge study, designed to test the ability of NOX-H94 to block hepcidin-mediated hypoferraemia in healthy volunteers. A Phase IIa study of NOX-H94 in myeloma and lymphoma patients with anemia is planned to start in the second half of 2012. Heparidin is the key regulator of iron metabolism and a mediator of iron restriction in anemia of chronic disease.

The Spiegelmer<sup>®</sup> platform provides the company with powerful and unique discovery capabilities, which have generated a number of additional leads under preclinical investigation. Located in Berlin, Germany, NOXXON is a well-financed mature biotech company with a strong syndicate of international investors, approx. 60 employees and a highly experienced management team. For more information, please visit: [www.noxxon.com](http://www.noxxon.com)

### About NOX-A12

NOX-A12 specifically binds and neutralizes CXCL12/SDF-1 (CXC chemokine ligand 12 / Stromal Cell-Derived Factor-1), a chemokine which activates and attracts immune and non-immune cells including stem cells from the bone marrow. CXCL12 binds with high affinity to two chemokine receptors, CXCR4 and CXCR7. The CXCL12 / CXCR4 / CXCR7 axis has been shown to play a role in stem cell mobilization, vasculogenesis, tumor growth and metastasis. Inhibition of CXCL12 binding to its receptors sensitizes tumor cells to chemotherapy and in some solid tumors, prevents invasion and metastasis, suggesting that NOX-A12 in combination with chemotherapy could be beneficial in the treatment of various cancers.

NOX-A12 has shown promising activity in models of both hematological and solid tumors in addition to models of stem cell mobilization. NOXXON's collaborators have shown that in multiple myeloma models NOX-A12 detached myeloma cells from stromal cells and sensitized them to killing by Velcade<sup>®</sup>/bortezomib both *in vitro* and *in vivo*<sup>2</sup>. NOX-A12 has also been shown to inhibit chemotaxis of patient-derived primary CLL cells towards higher concentrations of CXCL12 and to have distinct properties from CXCR4 antagonists<sup>3</sup>. In an animal model of glioblastoma, NOX-A12 treatment resulted in a significant extension of lifespan of animals when used in combination with radiation therapy<sup>4</sup>.

In Phase I studies with healthy volunteers, single doses of NOX-A12 up to 10.8 mg/kg and daily doses up to 2 mg/kg for five days were found to be safe and well tolerated and resulted in dose-dependent mobilization of white blood cells and CD34<sup>+</sup> hematopoietic stem cells as predicted by preclinical studies.

NOXXON received grant support within the program "KMU-innovativ" from the German Federal Ministry of Education and Research (BMBF) for the preclinical program and the Phase I clinical trials with NOX-A12.

Further information about the ongoing NOX-A12 Phase IIa clinical trials is available at ClinicalTrials.gov: relapsed MM (ID: NCT01521533) and relapsed CLL (ID: NCT01486797).

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<sup>2</sup> Roccaro AM (2011) ASH 53<sup>rd</sup> Annual Meeting, oral presentation 887, Session 652

<sup>3</sup> Hoellenriegel J (2011) ASH 53<sup>rd</sup> Annual Meeting, poster 3878, Session 652

<sup>4</sup> C. Liu (2012) AACR, Apr 3rd 2012 (abstract # 4382)