PRESS RELEASE

Cell Reports Publication on the Mechanism of Action of NOXXON's Anti-SDF-1 Spiegelmer® Olaptesed Pegol (NOX-A12) in Preclinical Multiple Myeloma Models

Berlin, Germany and Boston, USA - 26 September 2014 - NOXXON Pharma announced today the publication of a new study in *Cell Reports*, entitled "*SDF-1 Inhibition Targets the Bone Marrow Niche for Cancer Therapy".* The study of the hematological malignancy multiple myeloma in a mouse model was conducted by scientists from Dana-Farber Cancer Institute at Harvard Medical School, Boston, USA and NOXXON Pharma.

Metastasis, the process of tumors spreading and colonizing distant parts of the body, is one of the most deadly aspects of cancer. Traditionally, researchers have focused on the cancer cells themselves, however, the interactions between tumor cells and the tissues around them, the so-called microenvironment, is attracting increasing attention.

Dr. Irene Ghobrial, Associate Professor of Medicine at Harvard Medical School and her team, discovered that there is a high expression of a tumor cell-attracting messenger protein called stromal cell derived factor-1 (SDF-1/CXCL12) in bone marrow of patients with active multiple myeloma as well as in metastatic bone marrow niches of patients with solid malignancies. The Spiegelmer® olaptesed pegol (a PEGylated mirror-image (L-)oligonucleotide) was identified at NOXXON Pharma to bind tightly and specifically to SDF-1. It was hypothesized that blocking SDF-1 with olaptesed pegol could lead to a less alluring signal coming from bone marrow niches, thereby attracting fewer tumor cells. Indeed, olaptesed pegol treatment resulted in a decrease of disease progression and a prolonged survival in translational mouse models of multiple myeloma.

Dr. Aldo Roccaro, the study's co-first author with Dana-Farber colleague Antonio Sacco, said: "We know that myeloma cells can't survive for long if they are circulating in the blood and can't adhere to other tissue, so we think that neutralizing SDF-1 could change the bone marrow environment to make it less receptive for multiple myeloma cells, reduce myeloma cells' affinity for the marrow, and thereby inhibit the progression of the disease."

Senior author Dr. Irene Ghobrial added: "Metastasis remains one of the most important complications we face as physicians and cancer researchers, but our findings clearly document a therapeutic effect of olaptesed pegol in a mouse model of advanced myeloma."

Dr. Matthias Baumann, Chief Medical Officer of NOXXON Pharma, concluded: "These results suggest that targeting SDF-1 may represent a valid strategy to prevent or disrupt bone marrow colonization by multiple myeloma cells and possibly other tumors. In conjunction with interim results of our ongoing Phase IIa studies in multiple myeloma

and chronic lymphocytic leukemia, these findings further support the therapeutic potential of olaptesed pegol."

To access the (online) publication in *Cell Reports*, please follow this link: [http://www.cell.com/cell-reports/pdf/S2211-1247(14)00718-9.pdf]

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Notes for Editors:

About Multiple Myeloma
Multiple myeloma 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), multiple myeloma is the second most common blood cancer in the United States and accounts for approximately one percent of all cancers.

About Dana-Farber Cancer Institute
Dana-Farber Cancer Institute, a principal teaching affiliate of Harvard Medical School, is world-renowned for its leadership in adult and pediatric cancer treatment and research. Designated as a comprehensive cancer center by the NCI, it is one of the largest recipients among independent hospitals of NCI and National Institutes of Health grant funding.
For more information, please visit www.dana-farber.org

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

- Emapticap pegol (NOX-E36), an anti-CCL2/MCP-1 (C-C chemokine ligand 2 / Monocyte Chemoattractant Protein-1) Spiegelmer®, has completed a Phase IIa proof-of-concept study in patients with type 2 diabetes with albuminuria and a Phase IIb study is in the planning stages. CCL2 is a pro-inflammatory chemokine involved in the recruitment of immune cells to inflamed tissues.
- Olaptesed pegol (NOX-A12), an anti-CXCL12/SDF-1 (CXC chemokine ligand 12 / Stromal Cell-Derived Factor-1) Spiegelmer®, is currently being tested in Phase IIa studies in two hematological cancers, multiple myeloma (MM) and chronic lymphocytic leukemia (CLL). Studies for treatment of glioblastoma have also been designed and olaptesed pegol has received Orphan Drug Designation from the FDA for this indication. CXCL12 is a chemokine known to be involved in tumor invasion, metastasis, and resistance to therapy.
- Lexaptepid pegol (NOX-H94), an anti-hepcidin Spiegelmer®, has completed a Phase IIa pilot study in cancer patients with anemia and is now being studied in EPO-hyporesponsive dialysis patients. Hepcidin is the key regulator of iron metabolism and responsible for the iron restriction leading to anemia of chronic disease.

The Spiegelmer® 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, and approximately 60 employees.

For more information, please visit: www.noxxon.com

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