**PRESS RELEASE**

# NOXXON Initiates Phase IIa of anti-CCL2/MCP-1 Spiegelmer® NOX-E36 for Treatment of Diabetic Nephropathy

**Berlin, Germany- 19 June 2012**- NOXXON Pharma today announced the treatment of the first patient in a Phase IIa clinical trial of its anti-CCL2/MCP-1 (C-C Chemokine Ligand 2 or Monocyte Chemoattractant Protein-1) Spiegelmer® NOX-E36 in patients with diabetic nephropathy. About 1 in 3 patients with diabetes mellitus develops diabetic nephropathy, a progressive kidney disease that is one of the main causes of end-stage renal disease and the need for dialysis. The recruitment of immune cells by the chemokine CCL2 into the kidney along with direct effects of CCL2 on cells of the kidney are believed to be important in the progression of this disease.

NOXXON Pharma's multi-center, double-blind study will be conducted on 75 patients with Type II diabetes mellitus and albuminuria with a treatment duration of 12 weeks. 50 patients will be administered subcutaneous doses of 0.5 mg/kg of NOX-E36 twice weekly and the remaining 25 patients will receive placebo. The dose choice of 0.5 mg/kg of NOX-E36 is based on data from an earlier Phase Ib study which evaluated the pharmacodynamic effects of three different doses of NOX-E36 in diabetics during four weeks of treatment. All patients in the Phase IIa study will also be on the current standard of care to control hypertension, hyperglycemia and dyslipidemia.

The study will evaluate efficacy, PK, safety and tolerability of treatment with NOX-E36. The primary efficacy analysis will be based on a change from baseline in the albumin to creatinine ratio (ACR); renal, glycemic and inflammatory efficacy markers will also be followed during the trial. Interim evaluation of primary and secondary efficacy parameters is planned following completion of treatment of 25, 50 and 75 patients.

NOX-E36's mode of action is to specifically bind and neutralize the pro-inflammatory chemokine CCL2/MCP-1. This protein recruits immune cells to sites of inflammation and it plays an important role in complications of type 2 diabetes through recruitment of immune cells to adipose tissue, pancreatic islets and the kidney. CCL2 also triggers down-regulation of the protein nephrin, a key component of the renal filtration apparatus expressed by the kidney's podocyte cells. Inhibition of CCL2 is thus anticipated to be of benefit for type 2 diabetes patients with nephropathy. Preclinical studies have demonstrated that treatment with a Spiegelmer® CCL2 inhibitor can significantly delay the decline in kidney function as well as disease progression in animal models of diabetes.

This phase IIa study is the fourth clinical study of NOX-E36 that NOXXON Pharma has initiated and the Company is building up a positive bank of data supporting this product's potential in treating subjects with renal impairment. NOXXON plans to provide interim results from this trial later this year.

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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:

- NOX-E36 targets the pro-inflammatory chemokine CCL2/MCP-1 (C-C Chemokine Ligand 2 or Monocyte Chemoattractant Protein-1), and is currently in a Phase Phase IIa study in diabetics with albuminuria.

- NOX-A12 targets CXCL12/SDF-1 (CXC Chemokine Ligand 12 / Stromal Derived Factor 1), a chemokine mediator of tumor invasion, metastasis and resistance to chemotherapy, and has completed Phase I. Phase IIa studies in two hematological cancers, multiple myeloma and chronic lymphocytic leukemia have begun recruiting patients.
- NOX-H94 targets hepcidin, the key regulator of iron metabolism and mediator of iron restriction in anemia of chronic disease. A comprehensive single and multiple ascending dose Phase I study and an endotoxin challenge study, designed to test the ability of NOX-H94 to block hepcidin mediated hypoferremia, have both been completed are currently being analyzed. A Phase IIa study of NOX-H94 in myeloma and lymphoma patients with anemia is planned to start mid-2012.

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, approx. 60 employees and a highly experienced management team.

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

**About NOX-E36 and diabetic nephropathy**

NOX-E36 is a new therapeutic that specifically binds and neutralizes the pro-inflammatory chemokine CCL2, which is also known as monocyte chemoattractant protein-1 (MCP-1). CCL2 is involved in recruitment of monocytes to inflamed tissues where they differentiate into macrophages. Infiltration of monocytes/macrophages into the kidney is a hallmark of diabetic nephropathy[i]. Kidney macrophage accumulation is associated with progression of diabetes (hyperglycemia, HbA1c), development of renal injury (tissue damage, albuminuria), kidney fibrosis and decline in GFR (glomerular filtration rate), suggesting that inflammation promotes the disease[ii]. Activated macrophages release lysosomal enzymes, nitric oxide (NO), reactive oxygen species (ROS), and transforming growth factor beta (TGF-β) which play an important role in renal damage[iii].

Studies in diabetic mice have shown that macrophages account for almost all kidney leukocyte accumulation; their accrual correlates with both the progression of diabetes and the severity of kidney damage[iv]. Both experimental and clinical evidence supports the hypothesis that DN is an inflammatory disease prompted by a deranged metabolism[v].

The glomerular epithelial cells called podocytes are an essential component of the filtration barrier of the kidney. The podocytes form a tight web with their interdigitating foot processes joined by a specialized filtration structure called the slit diaphragm, a key component of which is the protein nephrin[vi]. Podocytes also express the receptor for CCL2, CCR2, and respond to CCL2 stimulus by cytoskeletal re-organization, increased motility and down-regulation of nephrin[vii]. These changes to the filtration apparatus of the kidney offer a potential explanation for the association of CCL2 and the leakiness that results in proteinuria in human diabetes.

Previously completed studies in animal models demonstrate that treatment with a Spiegelmer® CCL2 inhibitor show renoprotective effects in models of diabetic nephropathy and lupus nephritis[viii].

Based on epidemiological data from the International Diabetes Foundation and the US Centers for Disease Control, NOXXON estimates that there are approximately 9 million patients with Diabetic Nephropathy in the US, 7 million in Europe and 2 million in Japan. A recent analysis of 3,431 diabetes patients in the UK showed that the rate of decline of kidney function correlates with the amount of albumin in the urine. In this study diabetic patients with microalbuminuria (30-300 mg albumin / g creatinine) lost on average 1.5 % of their kidney filtration capacity per year, while those with macroalbuminuria (>300mg albumin / g creatinine) lost on average 5.7 % of their kidney filtration capacity per year[ix].

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