PRESS RELEASE

NOXXON Pharma Completes Patient Recruitment for Phase IIa Study in Diabetic Nephropathy

Promising Interim Efficacy Analysis of anti-CCL2 /MCP-1 Spiegelmer® NOX-E36

Berlin, Germany - 24 July 2013 - NOXXON Pharma today announced the successful completion of patient recruitment of its NOX-E36 Phase IIa clinical trial for the treatment of diabetic nephropathy. NOX-E36 is a Spiegelmer® that binds and neutralizes CCL2/MCP-1 (C-C Chemokine Ligand / Monocyte Chemoattractant Protein-1), a pro-inflammatory chemokine that plays an important role in the progression of diabetic nephropathy, the most common single cause of chronic kidney failure and end-stage renal disease.

The objective of this randomized, double-blind placebo-controlled Phase IIa study is to evaluate the efficacy, pharmacokinetics, safety and tolerability of treatment with NOX-E36. It has now enrolled the targeted 75 patients with type 2 diabetes mellitus and albuminuria who will be treated for 12 weeks with twice-weekly subcutaneous doses of NOX-E36 (50 patients) or placebo (25 patients). All patients are also treated with the current standard of care to control hypertension, hyperglycemia and dyslipidemia. This regimen includes stable renin-angiotensin system blockade, which has been demonstrated in randomized controlled trials to reduce the rate of progression of diabetic nephropathy in type 2 diabetics with hypertension, elevated serum creatinine and albuminuria.

The planned interim efficacy analysis of the first third of patients completing therapy in this Phase IIa study has now been completed with promising results. The primary efficacy analysis is based on the change in albuminuria from baseline at the end of the treatment period, expressed as albumin to creatinine ratio (ACR). Further analyses of efficacy parameters will occur following treatment of 51 and 75 patients. In addition to renal parameters, glycemic and inflammatory markers are being followed during the trial.

Dr. Matthias Baumann, Chief Medical Officer of NOXXON Pharma remarked: “We are very pleased with the excellent safety and tolerability seen so far in the study. Recently increased patient recruitment will allow efficacy analysis of all 75 patients later this year and full analysis of the study in early 2014. We plan to present interim results at one of the upcoming major international scientific conferences.”

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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 chemically synthesized L-stereoisomer oligonucleotide aptamers, a non-immunogenic alternative to antibodies. NOXXON has a diversified portfolio of clinical-stage Spiegelmer® therapeutics:

- NOX-E36, an anti-CCL2/MCP-1 (C-C chemokine ligand 2 / Monocyte Chemoattractant Protein-1) Spiegelmer®, is currently in a Phase IIa study in patients with type 2 diabetes with albuminuria. CCL2 is a pro-inflammatory chemokine involved in the recruitment of immune cells to inflamed tissues.
- NOX-A12, an anti-CXCL12/SDF-1 (CXC chemokine ligand 12 / Stromal Cell-Derived Factor-1) Spiegelmer®, 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 therapy.
- NOX-H94, an anti-hepcidin Spiegelmer®, is currently in a Phase IIa study in cancer patients with anemia. 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

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 the 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 support the hypothesis that diabetic nephropathy 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 resulting in proteinuria in human diabetes.

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

Poor glycemic control is associated with more rapid progression of diabetic nephropathy[ix]. It has also been shown that type 2 diabetic patients with poor glycemic control are significantly more likely to suffer from progressively increasing risks of coronary heart disease, cardiovascular disease and total mortality[x]. CCL2 expression has been correlated with glycemic control in certain populations[xi]. As such, neutralization of CCL2 may improve metabolic parameters; potentially further reducing the risk of progression in diabetic patients.

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 (>300 mg albumin/g creatinine) lost on average 5.7% of their kidney filtration capacity per year[xii].

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