



Two Presentations at International Conferences of Preclinical Data on NOXXON's anti-C5a Spiegelmer[®], a Potential Drug in Pneumococcal Pneumonia-Induced Sepsis

Berlin, Germany - 04 September 2014 - Scientists of Charité - Universitätsmedizin Berlin and NOXXON Pharma are invited to present new preclinical data about effects of NOX-D19, a Spiegelmer[®] neutralizing the complement component C5a, in pneumococcal pneumonia-induced sepsis.

The talks with the title "Neutralizing the Complement Component C5a Protects Against Lung Injury and Extrapulmonary Organ Injury in Pneumococcal Pneumonia-Induced Sepsis" will be held by Dr. Holger Mueller-Redetzky on Sunday, September 7 (Session 150) at the annual *European Respiratory Society International Congress* in Munich and by Dr. Axel Vater at the *XXV International Complement Workshop* in Rio de Janeiro on Tuesday, September 16 during Session V.

Severe community-acquired pneumonia is mostly caused by *Streptococcus pneumoniae* and often leads to sepsis with high lethality despite adequate antibiotic treatment. The likely reason for the unfavorable outcome is an uncontrolled inflammatory host response that causes additional injury to the lung and subsequently other organs.

NOX-D19, a PEGylated L-RNA aptamer (Spiegelmer[®]) binds and neutralizes the complement fragment C5a, a major mediator of the complement system which is involved in the immune response against infections but also contributes to hyperinflammation, vascular barrier dysfunction, microcirculatory failure, and organ failure. Hypothetically the inhibition of C5a-signaling by NOX-D19 in pneumococcal pneumonia could prevent pulmonary vascular barrier failure and protect against extrapulmonary organ failure.

The preclinical studies involving *Streptococcus pneumoniae*-infected mice were performed by Dr. Holger Mueller-Redetzky, Prof. Dr. Martin Witzernath and coworkers at the Department of Infectious Diseases and Pulmonary Medicine at the Charité - Universitätsmedizin Berlin in cooperation with the Institute of Anatomy and Cell Biology and the Institute for Clinical and Experimental Surgery at the Faculty of Medicine of Saarland University in Homburg. Mice were infected with *Streptococcus pneumoniae* and the Spiegelmer[®] NOX-D19 was applied at the time of infection and 24 hours later. The pulmonary permeability, pulmonary and blood leukocyte count, and levels of IL-1 β , G-CSF, KC and IL-6, bacterial load in lung, spleen and blood, markers of liver and kidney function (AST, BUN) and histological analyses of fibrin deposition and apoptosis in the liver were analyzed.

24 hours after infection, C5a levels reached a maximum in lung and blood. Lung failure and septic extrapulmonary organ injury developed within 48 hours post infection, as well as apoptosis of hepatocytes and microcirculatory failure. In contrast, in mice that

received NOX-D19, neutralization of the pro-inflammatory factor C5a attenuated pulmonary permeability and reduced blood cytokine levels. Furthermore protection from liver injury was observed.

The senior investigator of the study Prof. Dr. Martin Witzernath from Charité - Universitätsmedizin Berlin, concluded: "These first results in animal models are very promising. NOX-D19 seems to effectively neutralize C5a and have an effect on the overwhelming immune response that leads to unnecessary damage. NOX-D19 could thus give protection against lung and extra-pulmonary organ failure in pneumococcal pneumonia-induced sepsis and may offer an important adjuvant treatment strategy for improved survival in pneumococcal sepsis."

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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:

- 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.
- Olaptosed pegol (NOX-A12), an anti-CXCL12/SDF-1 (CXC chemokine ligand 12 / Stromal Cell-Derived Factor-1) Spiegelmer[®], is currently tested in Phase IIa studies in two hematological cancers, multiple myeloma (MM) and chronic lymphocytic leukemia (CLL). A study for treatment of glioblastoma has been designed. 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. Heparin 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, besides the anti-C5a Spiegelmer[®], 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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