

## PRESS RELEASE



### **Interim Phase IIa Results for Spiegelmer<sup>®</sup> Olaptosed Pegol (NOX-A12) in CLL and MM Studies**

*Five posters on NOXXON compound at 2013 American Society of Hematology (ASH) conference*

**Berlin, Germany - 09 December 2013** - NOXXON Pharma disclosed interim data from two independent clinical phase IIa studies of the anti-CXCL12/SDF-1 Spiegelmer<sup>®</sup> olaptosed pegol (NOX-A12) at the 55<sup>th</sup> annual meeting of the American Society of Hematology (ASH) in New Orleans, LA, USA from 7-10 December 2013.

In the first study, olaptosed was administered to relapsed chronic lymphocytic leukemia (CLL) patients in combination with bendamustine and rituximab. In the second study, olaptosed was combined with bortezomib and dexamethasone in patients with relapsed multiple myeloma (MM). Data from the 9 patient pilot groups in each study were presented.

In the trial focusing on relapsed CLL, olaptosed treatment resulted in an effective and prolonged mobilization of CLL cells into the peripheral blood. This mobilization reflects olaptosed's ability to block tumor-microenvironment interactions, which is thought to increase tumor cell sensitivity to killing by chemotherapeutic agents. In addition, the 100% overall response rate (ORR) and 22% complete response (CR) rate as well as the virtual absence of additional toxicity on top of the treatment with bendamustine and rituximab (BR) observed in this pilot group compares very favorably with historical controls. Provided that this promising clinical picture is maintained in the total sample of 33 patients, NOXXON plans to further develop this novel anti-CXCL12/SDF-1 Spiegelmer<sup>®</sup>.

In patients with relapsed MM, anti-CXCL12/SDF-1 Spiegelmer<sup>®</sup> olaptosed showed the same effect of mobilization of plasma cells into the peripheral blood. In addition, an overall response rate (ORR) of 67% including 22% very good partial responses (vgPR) was achieved in this pilot group. Importantly, treatment with olaptosed was not associated with additional toxicity on top of Velcade<sup>®</sup>/bortezomib and dexamethasone (VD). If these preliminary results can be maintained in the total sample of 28 patients, then again further development of this novel anti-CXCL12/SDF-1 Spiegelmer<sup>®</sup> will be warranted.

The titles and contributors for the two above mentioned poster presentations at ASH are as follows:

- Saturday, December 7, 5:30 PM - 7:30 PM, Hall E; Session 642, Publication number: 1635  
**Anti-CXCL12/SDF-1 Spiegelmer<sup>®</sup> NOX-A12 Alone and In Combination With Bendamustine and Rituximab In Patients With Relapsed Chronic Lymphocytic Leukemia (CLL): Results From A Phase IIa Study**  
*Marco Gobbi, Michael Steurer, Federico Caligaris-Cappio, Marco Montillo, Ann Janssens, Livio Trentin, Thomas Dümmler, Stefan Zöllner, Stefan Zeitler, Kai Riecke, Anna Kruschinski*

- Saturday, December 7, 5:30 PM - 7:30 PM, Hall G, Session 653, Publication number: 1951  
**Anti-CXCL12/SDF-1 Spiegelmer® NOX-A12 Alone and In Combination with Bortezomib and Dexamethasone In Patients With Relapsed Multiple Myeloma: Results From A Phase IIa Study**  
*Heinz Ludwig, Katja Weisel, Monika Engelhardt, Richard Greil, Anna Maria Cafro, Maria Teresa Petrucci, Thomas Dümmler, Stefan Zöllner, Stefan Zeittler, Kai Riecke, Anna Kruschinski*

Three more poster presentations at ASH have the following titles and contributors:

- Sunday, December 8, 6:30 PM - 8:30 PM, Hall E, Session 506, Publication Number: 2454  
**SDF-1 Inhibition Using Spiegelmer® NOX-A12 as a Novel Strategy for Targeting AML Cells Within their BM Microenvironment**  
*Rodrigo Jacamo, Zhihong Zeng, Ye Chen, Yuexi Shi, Teresa McQueen, Anna Kruschinski, Marina Konopleva, Peter P. Ruvolo, Michael Andreeff*
- Monday, December 9, 6:00 PM - 8:00 PM, Hall E, Session 604, Publication Number: 3851  
**Targeting the Protective Microenvironment in Multiple Myeloma (MM): An Analysis of The CXCL12/CXCR4-Axis and its Inhibitors AMD3100 and NOX-A12 Combined with Antimyeloma Substances, Such As Pomalidomide and Carfilzomib**  
*Anna Simon, Dagmar Wider, Marie Follo, Johannes Waldschmidt, Martina Kleber, Ralph Waesch, Monika Engelhardt*
- Monday, December 9, 6:00 PM - 8:00 PM, Hall E, Session 641, Publication Number: 4111  
**The Spiegelmer® NOX-A12 Abrogates Homing of Human CLL Cells To Bone Marrow and Mobilizes Murine CLL Cells in the Eμ-TCL1 Transgenic Mouse Model Of CLL**  
*Elisabeth Hinterseer, Tamara Girbl, Evelyn Hutterer, Petra Berghammer, Sylvia Ganghammer, Eveline Sift, Josefina Pinon Hofbauer, Alexander Egle, Anna Kruschinski, Richard Greil, Tanja Nicole Hartmann*

Members of NOXXON's drug development team and collaboration partners will be at the ASH conference to explain the mode of action and clinical potential of this innovative drug candidate.

- Ends -

## Notes for editors:

### About NOXXON Pharma AG

NOXXON Pharma AG is a biopharmaceutical company pioneering the development of a new class of proprietary therapeutics called Spiegelmers, which are chemically synthesized L-stereoisomer RNA aptamers and a non-immunogenic alternative to antibodies. NOXXON is approaching completion of multiple proof-of-concept studies with a diversified portfolio of clinical-stage Spiegelmer® therapeutics displaying good safety, tolerability and promising signs of efficacy:

- Emapticap pegol (NOX-E36), an anti-CCL2/MCP-1 Spiegelmer®, is currently in a Phase IIa study in patients with diabetic nephropathy. Interim data analysis suggests a positive influence on albuminuria and glycemic control.
- Olaptosed pegol (NOX-A12), an anti-CXCL12/SDF-1 Spiegelmer®, is currently in Phase IIa studies in two hematological cancers, multiple myeloma (MM) and chronic lymphocytic leukemia (CLL). Results to date have shown that olaptosed

neutralizes CXCL12 which leads to the mobilization of cancer cells in patients. Current clinical tumor response data and the very benign safety profile compare favorably with historical controls.

- Lixaptepid pegol (NOX-H94), an anti-hepcidin Spiegelmer<sup>®</sup>, has shown efficacy in a subset of anemic cancer patients with functional iron deficiency in a pilot study where pharmacodynamic parameters of iron metabolism and erythropoiesis were positively influenced and hemoglobin levels increased following lixaptepid mono-therapy. The product will also be evaluated in a Phase IIa study in dialysis patients with ESA-hyporesponsive anemia.

The proprietary Spiegelmer<sup>®</sup> platform provides NOXXON with powerful and unique discovery capabilities, which have generated a number of additional leads such as NOX-S93, NOX-G15, NOX-D20 and NOX-L41 in the fields of inflammation, diabetes, metastasis and pain.

Located in Berlin, Germany, NOXXON is a well-financed mature biotech company with a strong syndicate of international investors, and approximately 60 employees.

### **About olaptosed pegol (NOX-A12)**

Olaptosed 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 disrupts tumor-microenvironment interactions thereby sensitizing tumor cells to therapy as well as preventing invasion and metastasis in some solid tumors. This suggests that olaptosed in combination therapies could be beneficial in the treatment of various hemtological and solid malignancies.

Indeed, olaptosed 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 olaptosed detached myeloma cells from stromal cells and sensitized them to killing by Velcade<sup>®</sup>/bortezomib both *in vitro* and *in vivo*<sup>1</sup>. Olaptosed 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>2</sup>. In an animal model of glioblastoma, olaptosed treatment resulted in a significant extension of lifespan of animals when used in combination with radiation therapy<sup>3</sup>.

In Phase I studies with healthy volunteers, single doses of olaptosed 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.

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<sup>1</sup> Roccaro AM (2011) ASH 53<sup>rd</sup> Annual Meeting, oral presentation 887, Session 652

<sup>2</sup> Hoellenriegel J & Zboralski D, et al., Blood 2013 Nov 25.

<sup>3</sup> Liu S-C et al., Neuro Oncol 2013 (in press)

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

**Contact:**

<b>NOXXON Pharma AG</b>	<b>College Hill Life Sciences</b>
Emmanuelle Delabre T: +49-30-726247-0 <a href="mailto:edelabre@noxxon.com">edelabre@noxxon.com</a>	Robert Mayer / Cora Kaiser T: +49-89-57001806 <a href="mailto:noxxon@collegehill.com">noxxon@collegehill.com</a>