

## Press Release

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### Phenex initiates Phase I first-in-man study with its clinical development candidate Px-102

*The FXR agonist Px-102 might open new avenues for the treatment of Non-Alcoholic Steatohepatitis (NASH) and other severe liver diseases*

Ludwigshafen, September 15th, 2011

Phenex Pharmaceuticals AG announced today the start of a first-in-man Phase I study with its clinical drug candidate Px-102, a synthetic non-steroidal FXR agonist. The volunteers of the first dose level received the drug and showed no signs of discomfort or other adverse effects. This Phase I first-in-man study will be escalated from the initial dose over seven dose levels to obtain information about the tolerance and pharmacokinetics of Px-102 in healthy volunteers. Following this first Phase I study Phenex plans to run a multiple ascending dose Phase I study where the same parameters will be observed during several days of multiple administrations. The Phase I studies for Px-102 will be finished by early 2012. If all requirements are met, Phenex then plans to test Px-102 in a Phase II study in patients with Metabolic Syndrome and Non-Alcoholic Fatty Liver Disease (NAFLD) to confirm if the potent therapeutic effects such as lipid lowering, improvement of insulin sensitivity and reduction of markers for liver damage which were observed in several animal studies can be reproduced in human patients

Px-102 is a potent, fully-synthetic and non-steroidal FXR agonist. The Farnesoid X Receptor (FXR) is a bile acid receptor which when activated by Px-102 has a profound positive impact on cholesterol, triglyceride and glucose metabolism in liver and intestine.

As was already demonstrated in several publications and Phenex-proprietary animal studies the FXR agonist Px-102 potently reduces intestinal uptake of neutral lipids and cholesterol and at the same time enhances the excretion of these lipid species. In addition, Px-102 improves hepatic insulin sensitivity and shows massive hepatoprotective effects in animal models of liver cirrhosis or

fibrosis. It is this combination of potent metabolic and liver protective effects that makes Px-102 an ideal candidate for the treatment of Non-Alcoholic Steatohepatitis (NASH). Inflammation and beginning fibrosis are the hallmarks in people with NASH-livers which affects a subset of individuals who have developed a fatty liver due to an unhealthy lifestyle and overweight. The prevalence of NASH is estimated to approach 5% of the total population in industrialized countries. NASH markedly increases the likelihood to develop liver cancer or end stage liver cirrhosis. Currently there is no approved therapy for NASH.

„We aim at filling exactly this gap in medical treatment of liver diseases,“ says Dr. Claus Kremoser, CEO of Phenex. “NASH and associated liver and metabolic diseases are on the rise and there is no pharmacotherapy approved. Potent synthetic FXR-agonists such as Px-102 have the potential to improve the overall metabolic state as well as the inflammatory and fibrotic changes in livers of NASH patients. Next to the therapy of NASH itself, Px-102 may be well suited to treat related diseases such as liver cirrhosis and fibrosis, Primary Biliary Cirrhosis (PBC) or Portal Hypertension.”

#### **About Phenex Pharmaceuticals AG:**

Phenex is a privately held drug discovery and development company headquartered in Ludwigshafen with a research site in Heidelberg. The company focuses on novel attractive nuclear receptor targets to develop innovative small molecule therapeutics in the fields of metabolic syndrome / NASH and in autoimmune diseases.

Phenex' most advanced program is Px-102, now at Phase I clinical stage, and it targets the nuclear bile acid receptor FXR. This FXR agonist has unique properties in that it shows beneficial effects in lipid lowering, in improving insulin sensitivity, in reducing body weight and in ameliorating the liver inflammation and fibrosis that are hallmarks of Non-Alcoholic Steatohepatitis (NASH). NASH is a metabolically induced liver disease with a worldwide prevalence of at least 25 million affected individuals. If untreated, the disease can progress towards liver cirrhosis and liver failure or to Hepatocellular Carcinoma (HCC). There is no approved treatment for NASH. Px-102 addresses this medical need and represents a significant commercial opportunity.

Phenex' second R&D program targets the nuclear receptor ROR $\gamma$ t. ROR $\gamma$ t inhibitors hold the promise to become a new therapeutic approach in different autoimmune diseases with substantially reduced side effects. This project is at lead optimisation status.

The company intends to develop its R&D programs up to a proof-of-concept study in humans in the case of FXR and up to late preclinical stage in the case of ROR $\gamma$ t. At these stages the company will seek partners from the pharmaceutical industry to license these molecules for further development.

Phenex is financed through three consecutive rounds of funding bringing the total equity raised to 17,2 million Euros. The circle of investors encompasses EVP Capital Partners/VRP, LBBW Venture, Creathor Venture, KfW as well as private individuals and key persons from the pharmaceutical and high-tech industry.

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