Press Release

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Phenex reports successful completion of Phase I Studies with FXR-Agonist Px-102 and publishes research progress in two independent papers

On the back of the good scientific news, Phenex raises 5 Mio Euro in its fourth (Series D) financing round

Ludwigshafen, October 31st, 2012

Phenex Pharmaceuticals AG today announced the successful completion of its Phase I studies with Px-102, the company´s proprietary FXR agonist. Px-102 was tested in a single and in a multiple ascending dose Phase I study in 54 and 42 healthy volunteers, respectively. The drug candidate was safe and well tolerated at all doses indicated. Additional detailed data on the beneficial effects of Px-102 in animal models of lipid lowering and in preventing tumor growth in a liver cancer model were published by Phenex senior authors in the *Journal of Experimental Therapeutics and Pharmacology (Hambruch et al, JPET, epub Aug 23, 2012)* and in *PLOSone (Deuschle et al. PLOSone 7(10) e43044, 2012)*.

The published data underscore that the massive cholesterol lowering effects of Px-102 observed in various animal models including primates, results in the prevention of atherosclerosis in a standard mouse model (*JPET* paper). The accumulation of free cholesterol in the liver is believed to be a main driving force for NASH (Non-Alcoholic Steatohepatitis, see “About Phenex”) thus cholesterol lowering will contribute to the overall hepatoprotective effects of Px-102.
Given that Px-102 will be developed as a novel treatment for NAFLD and NASH, it was also important to investigate if the lipid lowering and other hepatoprotective effects observed so far might also be useful in the prevention of liver cancer. In the *PLOSone* paper the Phenex authors show that multiple weeks of treatment with Px-102 inhibit tumor growth in a xenograft liver cancer model, probably via activation of a tumor suppressor gene, NDRG-2, which was identified as a novel target gene of FXR. The fact that Px-102 also effectively inhibits growth of liver tumors is relevant in a clinical setting where currently up to 5% of all NASH patients develop liver cancer over time so that the prevention of liver cancer is a main clinical goal in the treatment of NASH.
The outcome of the Phase I human studies combined with the published data from animal models provide encouraging evidence that the FXR agonist Px-102 will show beneficial effects in patients with NASH, a metabolically induced chronic inflammatory and fibrotic

disease of the liver.

These data together with the progress in Phenex´ second R&D program which targets RORgamma-t prompted Phenex existing investors to invest another 5 M Euro into Phenex. The additional funds will be earmarked for the further development of Px-102 and to broaden the ongoing RORgamma-t program.

“We want to back Phenex´ in its ongoing R&D programs to achieve an optimum position in its planned partnering activities”, explains Dr. Farsin Yadegardjam, Head of Phenex´ Supervisory Board and Managing Partner at EVP Capital Partners who manages the VRP fund which has financed Phenex from its first round on. “Phenex has successfully demonstrated its capabilities in preclinical research and early clinical development and we understand that more money helps creating more comprehensive data which furthers strengthens Phenex´ basis for negotiations in its outlicensing and partnering activities.”

Dr. Claus Kremoser, CEO of Phenex complements: “We are very pleased with these data since they demonstrated that our FXR agonist Px-102 has an enormous potential in gastrointestinal diseases beyond NASH, potentially even in the chemoprevention of liver cancer. And we are even more pleased that these good results strengthened the confidence of our investors into us so that we can further invest into both of our programs. Our RORgt inhibitor program which aims in developing a novel orally available drug for the treatment of autoimmune and chronic inflammatory diseases received great attention after the release of clinical study results with IL-17/IL17-R antibodies that showed the relevance of the RORgt/IL-17 pathway in patients with psoriasis. Thus, it deserves enhanced efforts to remain at the forefront of RORgt research and our investors have enabled us to do this by investing another 5 M Euro into us. We are very grateful for this commitment.”

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 liver diseases / NASH (FXR program) and in autoimmune diseases (RORgt program).

Phenex´ most advanced program is the FXR agonist Px-102 with which two phase I studies have just been finished. Px-102 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 is a hallmark 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 program at preclinical stage targets RORgamma-t. RORgamma-t (RORgt) is a Nuclear Receptor that was recently identified as a key differentiation factor of so-called Th-

17 cells, immune cells that produce and secrete Interleukin-17 which is believed to be a key player in chronic autoimmune-related inflammation. The relevance of the IL-17 pathway has been highlighted by the clinical success of the anti-IL-17 or the anti-IL-12/IL-23 antibodies that all have demonstrated superior efficacy in reducing symptoms in patients with moderate to severe psoriasis. RORgt binds endogenous small molecules and induces the production of IL-17, thus small molecule inhibitors of RORgt have the potential to block the IL-17 pathway in a similar fashion than the antibodies but with potentially fewer side effects combined with the typical advantages of a classical small molecule drug. The effectiveness of inhibiting the IL-17 pathway through small molecule RORgt inhibitors was recently demonstrated in animal models in two adjacent publications in *Nature*.

Phenex is now financed through four consecutive rounds of funding totalling the money raised to 22 million Euros. The circle of investors into Phenex encompasses EVP Capital Partners/VRP, LBBW Venture, Creathor Venture, CD Venture, KfW as well as private individuals and key persons from the pharmaceutical and high-tech industry.

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