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Plexxikon, Wyeth PPAR Deal: Up To \$372M In Diabetes Bid

By Randall Osborne
West Coast Editor

If there's anxiety lingering after the FDA's summer ruling about potential cancer toxicity with peroxisome proliferator-activated receptors (PPARs), you wouldn't know it from Wyeth – which entered a potential \$372 million deal with Plexxikon Inc. to develop treatments for diabetes and metabolic disorders.

The collaboration is focused on oral PLX204, which is the PPAR pan-agonist for Type II diabetes from privately held Plexxikon, of Berkeley, Calif.

“We started the project not even two years ago,” said Peter Hirth, Plexxikon's CEO. “This sets a new standard in drug discovery. I have not seen a process anywhere that has been so rapid,” involving fewer than 100 compounds from the initial hit in the screen before a candidate was

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Xcyte Raises \$26M Through Placement Of Preferred Stock

By Aaron Lorenzo
Senior Staff Writer

Xcyte Therapies Inc. grossed \$26 million through a public offering of 2.6 million preferred shares at \$10 apiece.

Officials at the Seattle company couldn't comment on the transaction due to SEC-imposed quiet-period rules, but in its prospectus, Xcyte said the funding would be used for working capital and general corporate purposes, such as clinical trial activities, preclinical research, manufacturing activities, capital expenditures and complementary technology acquisitions.

Its ongoing clinical activities include studies of its Xcellerated T Cell products in chronic lymphocytic leukemia, multiple myeloma and non-Hodgkin's lymphoma. Xcyte's T cell products stem from its Xcellerate

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Plexxikon

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found, he said, crediting the firm's crystallography approach.

Plexxikon had been planning to file an investigational new drug application this quarter "and we would have," Hirth told *BioWorld Today*. With the new partner, "there are more people to read and sign off, and the filing per se will take a little more time," he said.

Madison, N.J.-based Wyeth is paying more than \$22 million, including an up-front license fee and multiyear research funding, along with milestones that could total almost \$350 million as drugs are developed and commercialized. There also are royalties. Wyeth also will provide a loan to fund Plexxikon's share of clinical efforts.

Together the companies will develop PLX204, which modulates the function of three related targets – PPAR alpha, delta and gamma – thus potentially regulating levels of glucose, triglycerides, free fatty acids, HDL (the "good cholesterol") as well as energy expenditure, in a once-daily pill.

Plexxikon already has completed a single-dose pharmacokinetics study with the compound in humans, and follow-on compounds will be tailored to a subset of patients in the pre-diabetic and diabetic population.

PPARs on the market include London-based GlaxoSmithKline's Avandia (rosiglitazone) to control blood sugar in Type II diabetes and Actos (pioglitazone) for the same indication from Eli Lilly and Co., of Indianapolis. Many companies are trying to develop more, although in July the FDA threw a hurdle in front of San Diego-based Ligand Pharmaceuticals Inc., which had been planning a Phase III trial with naveglitazar, its PPAR formerly known as LY519818 for Type II diabetes. (See *BioWorld Today*, July 12, 2004.)

The regulatory agency said any PPAR trials scheduled to last longer than six months are not allowed to start until two-year rodent toxicity studies are finished and submitted to the agency for consideration – thus delaying naveglitazar, for 18 months to 24 months.

Rodent data reviewed by the FDA for a number of PPAR agonists (gamma, alpha or dual agonists, though not including naveglitazar) yielded unsafe carcinogenicity findings, and the six-month rule was put in place to alleviate concerns.

The cancer worries have made some pharmaceutical companies back out of the PPAR space entirely, but the likes of London-based AstraZeneca plc and Bristol-Myers Squibb Co., in New York, are marching ahead with programs.

In general, through the FDA rule, "everybody else's clock was reset to the time that we are [already] on," Hirth said.

PPARs have well-known applications outside of diabetes. Warner-Lambert Co., of Morris Plains, N.J. (now part of New York-based Pfizer Inc.) came up with the PPAR alpha drug Lopid (gemfibrozil), approved for lowering cholesterol in 1981. Later cleared for reducing heart-disease risk in some patients, the drug these days is available in generic form.

Mixing PPARs for their varied effects can lead to unexpected toxicity, so Plexxikon sought to combine the separate benefits in a single pill. Wyeth obviously was impressed and there's more to come, Hirth promised, citing a deep pipeline that might be of interest to other partners.

Kathleen Glaub, Plexxikon's president and chief financial officer, told *BioWorld Today* the parties trying for a piece of PLX204 were "quite competitive. We had multiple parties in negotiation, and we have a number of other discussions [for other programs] going on now."

A lean staff of about 50 employees means the company's burn rate is moderate, allowing for flexibility in making decisions about whether to collaborate, Hirth noted.

Said Glaub: "We don't have to sell the crown jewels of Plexxikon. We have assets we can take forward ourselves." ■