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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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Neuroscience 2004

Effects Impressive, Mechanism Elusive For Endocannabinoids

By Anette Breindl
Science Editor

SAN DIEGO – At first glance, the potential uses of endocannabinoid receptor manipulation look a bit like Every Flavor Beans, referenced in the Harry Potter books. At this year's annual meeting of the Society for Neuroscience, held here last week, research was presented that probed the role of endocannabinoids in such diverse subfields as amyotrophic lateral sclerosis, appetite regulation, convulsions, drug abuse, neural plasticity, pain, Parkinson's disease and traumatic brain injury – and that list is not comprehensive.

Add to that the fact that both agonists and antagonists are being described as beneficial – sometimes in the same poster session.

As receptor families go, the endocannabinoid one is
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Protein Sciences' FluBlok Moves To Phase II/III Work

By Karen Pihl-Carey
Staff Writer

A flu vaccine shortage might help companies like Protein Sciences Corp. accelerate their development plans for next-generation vaccines.

The Meriden, Conn.-based company received FDA clearance this week to conduct a Phase II/III proof-of-principle study of its patented cell culture influenza vaccine FluBlok.

The randomized, double-blind, placebo-controlled trial will enroll people between the ages of 18 and 49 and will compare two FluBlok doses with a placebo group.

"The primary purpose is to firmly establish our dose, and the second purpose is to establish efficacy," said Manon Cox, the company's chief operating officer, who expects to have results in May.

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FluBlok

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Cox and her colleagues at Protein Sciences are hoping, clinically speaking, for a relatively robust influenza season in 2004-2005. If there is at least a 10 percent attack rate throughout the U.S., the Phase II/III trial should be able to demonstrate statistical significance in terms of FluBlok's efficacy. If all goes well, Protein Sciences would move directly into a pivotal study in the following flu season, with hopes of having the vaccine on the market by the 2007-2008 season.

But it could happen sooner, if the FDA is satisfied with the efficacy results of the Phase II/III trial.

"It's possible," Cox told *BioWorld Today*, "the FDA could say to us, 'We don't want you to do another study. Just complete the safety database.'"

Researchers are enrolling patients at the University of Rochester in New York, the University of Cincinnati Children's Hospital and the University of Virginia. If it is an active influenza season, Protein Sciences has FDA permission to conduct two bridging studies next spring, one in children aged 6 months to 24 months, and the other in elderly patients.

FluBlok is the only vaccine under development that can resolve the issues associated with the licensed egg-grown vaccines, the company said. It could, therefore, address the entire influenza vaccine market, which is estimated at more than \$4 billion.

Earlier this month, Emeryville, Calif.-based Chiron Corp. said European authorities concerned about sterility issues suspended its license to manufacture Fluvirin in its Liverpool, UK, facility, the only Chiron facility approved to supply flu vaccine to the U.S. As a result, Chiron said it would not have any product ready for the 2004-2005 flu season, leaving the U.S. with a 50 percent shortage of supply. (See *BioWorld Today*, Oct. 6, 2004.)

"The rumors surrounding Chiron's vaccine is that the egg-based process is not a very sterile process," Cox said. "It's very complicated in these old factories to really keep these sterile."

The shortage has exposed a weakness in U.S. plans for flu vaccine, placing companies like Protein Sciences at the forefront. Daniel Adams, the company's president and CEO, said Protein Sciences is the only company conducting a late-stage cell-culture vaccine trial in the U.S.

FluBlok's antigens are developed using recombinant DNA technology and are manufactured in cell culture without eggs. Unlike licensed vaccines and other cell-culture vaccines in development, Protein Sciences does not use live influenza viruses, biocontainment facilities or harsh chemicals, such as formaldehyde, in its manufacturing. FluBlok consists solely of three antigens stored in sterile buffered salt water without preservatives such as the mercury derivative thimerosal.

"The biggest advantage is basically that our product only has the active ingredients," Cox said. "This product is

95 percent pure vs. the egg-based products or the cell-based products in development.

"There will be no thimerosal in our vaccine, no preservative," she added. "If you realize that 18 percent of the people are allergic to thimerosal, you can see that is also a major advantage."

The company's vaccines can be developed quickly and safely to address influenza viruses that appear late in the season, such as A Fujian did in the 2003-2004 season. Protein Sciences, for instance, made a vaccine for the 1997-1998 Hong Kong "bird" flu in just eight weeks.

"The big advantage of any cell culture-based approach, whether making an influenza virus or a recombinant protein, is you basically need to grow your cells, and you have a production schedule, and in a week you can turn out a batch," Cox said. "Eggs need to be ordered well in advance."

While Protein Sciences is funding the Phase II/III trial, the company is actively raising additional capital through New York-based Credit Suisse First Boston to support future trials and commercial manufacturing. The company also is considering partnering for manufacturing services, since raising a facility to produce bulk product of FluBlok would cost about \$30 million. It is likely the company will partner for the commercialization of the product. Cox said the company needs another source of income by the first quarter of 2005, and should have something in place by January.

The flu vaccine shortage in the U.S. might help Protein Sciences get the funds it needs.

"[The flu vaccine shortage] doesn't affect the timeline for this trial because we are on track," Cox said. "What it does affect is the interest of the venture capitalists and the financial community."

The National Institute of Allergy and Infectious Diseases sponsored seven previous trials of FluBlok that showed safety and the generation of antibody titers that are protective against influenza. The most recent trial conducted last flu season in about 400 elderly people compared a licensed egg-grown vaccine with three different doses of FluBlok containing the same hemagglutinin antigens. That data showed that all doses of FluBlok were safe and achieved antibody levels that might provide better protection against an H3 influenza virus than the licensed vaccine. While 30 percent to 50 percent of subjects vaccinated with the licensed vaccines historically achieve protective titers against the H3 strain, between 77 percent and 97 percent of patients vaccinated with the highest doses of FluBlok achieved protective titers, as measured by Geometric Mean Titer.

Founded in 1983, Protein Sciences is focused mostly on next-generation human and animal vaccines. Aside from FluBlok, the company has a SARS vaccine and an erythropoietin product that have completed animal tests and are scheduled to enter the clinic soon. All of its products are recombinant and are made using the company's protein expression technology, the baculovirus protein expression system. ■