



PDLI – SGEN – DNA
A Fruitful Collaboration

Protein Design Labs (PDLI) sublicensed to Genentech (DNA) development and commercialization rights for **antibody-drug conjugates directed against the PR1 antigen**, which is frequently differentially expressed in prostate cancer. **PDL will receive an upfront licensing fee, and is entitled to receive milestone payments and royalties on future.**

Protein Design has a broad collaboration agreement with **Seattle Genetics (SGEN)**. **This agreement gives the right to** PDLI to develop antibody-drug conjugates (ADCs) to certain targets, including PR1 antigen, chosen by Genentech

To kill cancer cells, antibodies directed against the PR1 antigen might need to be attached cell-killing agent such as the potent **auristatin derivatives** utilized in Seattle Genetics' ADC technology. By linking a drug to an antibody that targets PR1, it may be possible to identify new antibody-drug conjugate products to selectively kill prostate cancer cells while killing a lesser proportion of non-prostate cancer cells.

Research related to the preclinical validation of a PR1 ADC, anti-TMEFF2 monomethyl auristatin E-conjugated antibodies in the treatment of prostate cancer was published in the August 2004 edition of Molecular Cancer Therapeutics.

Mark McDade, Chief Executive Officer, PDL, believes that out licensing this program could be the most efficient way to continue its development.

*Seattle Genetics' second-generation ADC technology employs synthetic, highly potent drugs that can be attached to antibodies through **proprietary linker systems**. The linkers are designed to be stable in the bloodstream but to release the drug payload under specific conditions once inside target cells, potentially sparing non-target cells many of the toxic effects of traditional chemotherapy. ADCs can increase the therapeutic potential of the many antibodies that possess targeting ability but no inherent cell-killing activity.*

Genentech chooses the right targets. Protein Design and Seattle Genetics are equipped to deliver. It is good news for all of them.

EYETECH (EYET)

Eyetech now sees an increase in projected sales of Macugen to \$175 million and \$190 million for the year ending Dec. 31 from a prior projection of \$135 million to \$150 million during the period.

"Macugen's launch has exceeded our initial expectations and we are pleased that Macugen is quickly establishing itself as a foundation therapy for neovascular AMD: said David Guyer, the company's CEO, in a statement. According to Eyetech, retinal specialists are adopting Macugen faster than the firm had previously anticipated. An unexpected profitability could be realized in the latter half of the year.

Eyetech also said it expects to record a non-cash charge of between \$17 million and \$19 million in the next year related to a decision to accelerate the vesting of certain out-of-the-money stock options. Lower future expenses and realign employee incentives is the firm's strategy. It estimates the acceleration of the vesting will cut the charge related to expensing of unvested options by as much as \$61 million over the 40 months following the required implementation of new accounting rules.

Good news, of course, for EYET. Yet, we have not yet forgotten that the reason for the stock decline was not a lack of revenues or delayed profitability, but the outstanding data that came with the results of Genentech's competing drug Lucentis. When approved, Lucentis could represent a formidable competitor to Macugen, which would impact the long-term performance of Eyetech's drug.

MULTIPLE SCLEROSIS

IMMUNE RESPONSE (IMNR)

Preliminary clinical trial results show that its investigational vaccine **NeuroVax** restores immune cell activity in multiple sclerosis, or MS, patients to levels seen in healthy patients. In an ongoing clinical trial, MS patients given monthly injections of NeuroVax over one year had an increase in FOXP3, a gene marker that tracks T-cells. FOXP3 abnormalities are associated with unregulated T-cells in M.S. patients. The cells attack the fatty tissue that protects nerve fibers, causing a condition that results in movement and balance problems and impaired vision. The company said that patients given NeuroVax had more normal and regulated T-cell activity, reducing the immune system's attack on the nervous system.

This is early, but good news.

COLLABORATION

XOMA (XOMA) AND LEXICON GENETICS (LEXG)

LEXG's technologies identify pathways and targets and XOMA's technology provides the antibodies products that best act on these targets. The deal, which is set for three years, could be extended. Lexicon will get 65 percent of any profits and will bear 65 percent of the costs of the research, XOMA will share 35% of the cost and get the same from the revenues. The good news is that the partners have already selected the first target. It is intended to treat **type II diabetes, as well as obesity**. As part of the deal, Lexicon has promised to provide at least two other targets during the three years.

In the past few months, Xoma's technology has been validated three times by three firms resorting to its technology for developing antibody drugs. **Chiron** was the first to hand Xoma several targets, followed recently by **Merck** and now by the genomic firm **Lexicon Genetics**.

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