GTC. The primary endpoint for this new trial was the incidence of thromboembolism in 31 individuals (14 of whom came from the European trial, with 17 supplementary patients) with hereditary antithrombin deficiency who received ATryn for one week to prevent thromboembolism before, during or after surgery or childbirth compared with plasma-derived antithrombin-treated controls. Only one of the ATryn-treated participants developed a thromboembolus. Pooling the phase 3 and phase 2 data in a noninferiority trial design, the FDA accepted that ATryn was as effective as plasma-derived antithrombin-α.

The transgenic animal–produced protein is unlikely to be a financial windfall for GTC, however. ATryn is indicated for use in people with hereditary antithrombin deficiency, who are at high risk of blood clots during surgery and childbirth. Rodman and Renshaw of New York estimate that about 1,500 surgeries in the US and 3,500 in Europe require antithrombin therapy, and project a peak of $40–50 million annually in the US, perhaps double that worldwide. The firm predicts sales of $6–10 million in 2009. "It's not a game changer the second it comes out on the market, and I think it's going to take some time [to become accepted]. It hasn't had meaningful sales in Europe," says Reni Benjamin, managing director and senior biotech analyst with the firm, who admits that lagging sales in Europe might be due to insufficient marketing. "We want to see how well [GTC's partner, Ovation] will do at generating sales." Ovation Pharmaceuticals of Deerfield, Illinois, which was acquired by Danish pharma company H. Lundbeck of Copenhagen in February, has marketing rights to ATryn in the US.

ATryn will compete against a human plasma version of Thrombate III (antithrombin III), marketed by Talecris Biotherapeutics, located in Research Triangle Park, North Carolina. Thrombate III's efficacy is the same, says Benjamin, but the use of transgenic goats could make ATryn cheaper to produce. Human plasma products can also be a source of blood-borne diseases. Using transgenic goats "obviates that risk," says Benjamin.

GTC is also pursuing ATryn as a treatment for cases of heparin resistance. Individuals undergoing cardiopulmonary bypass are given heparin to prevent clotting during the procedure, but antithrombin can become depressed, blunting the drug's effectiveness. The company believes that supplementary ATryn could help restore antithrombin levels and circumvent heparin resistance. "That would be a much larger market," says Newberry.

The approval represents a first step for GTC, which will seek to apply its proprietary technology to the production of other drugs. "The value is in the proof and acceptance of their *in vivo* platform to produce therapeutic proteins," says Eric W. Overström, a professor of biology and biotech at Worcester Polytechnic Institute, in Worcester, Massachusetts, who collaborated with GTC on some of the original goat transgenic work but is no longer associated with the company.

GTC achieves expression of ATryn in milk by linking the antithrombin-α transgene to mammary-specific promoters of milk

Details

The companies have entered a collaboration to identify new drug targets and therapeutics across various disease areas. Under the terms of the agreement, Novartis will pay Epistem, a company commercializing its expertise in epithelial stem cells, $4 million up front and two years' worth of R&D support. Novartis has an option to exclusively license targets for biotherapeutic product development in exchange for license fees, milestone payments and royalties. The deal also includes up to $45 million in milestones for each new product developed. Epistem is also eligible to receive tiered royalties on global sales. Epistem's internal research, focused on the regulation of adult stem cells in epithelial tissues including gastrointestinal tract, skin, hair follicles, breast and prostate, will benefit from the pact.

Pfizer has agreed to license and evaluate Xencor's antibody optimization technologies. Pfizer will apply Xencor's Xtend technology to prolong antibody half-life and XmAb ADCC—enhancing technology to its antibody drug candidates in several discovery projects. Pfizer has also taken a commercial license for Xencor's technology for one program. Xencor will receive an up-front payment and is eligible to receive additional considerations based on the successful commercialization of products that incorporate its technologies.

The eight-year collaboration program will focus on drought tolerance and nitrogen utilization optimization in key crops such as corn and soybean (but the base crop of the project is obviously rice). ARRI researchers will use rice as a model to study novel gene functions, and will work closely with Syngenta's new biotech research and technology center in Beijing.

IN brief

RIP Raptiva?


Merck Serono

Merck Serono headquarters

The US Food and Drug Administration has issued a public health advisory on Genentech's psoriasis drug Raptiva following four cases and three confirmed deaths from progressive multifocal leukoencephalopathy (PML), a rare and usually fatal brain viral infection, in patients taking the drug for several years. In Europe and Canada, where the drug is marketed by Geneva-based Merck Serono and Serono of Mississauga, Ontario, respectively, regulators have taken Raptiva off the market, stating that the benefit did not justify the risk. This may be the last straw for Raptiva (efalizumab), a monoclonal antibody (mAb) directed against T-cell marker CD-11. "It's doomed," says Eric Schmidt, biotech analyst with Cowen and Company of New York. Raptiva, developed by Genentech of S. San Francisco, California, received a black box warning in 2005, after several cases of hemolytic anemia and again, in October 2008, following the first PML case. "Fortunately for Genentech it's a minor drug," garnering around $100 million annually, says Schmidt. Although Raptiva was the first biologic to reach the market for psoriasis, sales were quickly eclipsed by a trio of tumor necrosis factor-α inhibitors: Enbrel (etanercept) from Amgen of Thousand Oaks, California, Remicade (infliximab), from Centocor of Horsham, Pennsylvania and Humira (adalimumab), from Abbott of Abbott Park, Illinois. Centocor's mAb Stelara (ustekinumab), which targets IL-12 and IL-23, and recently approved in Europe, may further erode Raptiva's sales. This isn't the first time an immune modulating drug has been associated with PML. In 2005, the multiple sclerosis drug Tysabri (natalizumab) produced by Biogen-Idec of Cambridge, Massachusetts, and Elan of Dublin, a mAb targeting integrin, was voluntarily withdrawn from the market after two patients contracted PML; the companies later returned with a risk minimization plan. Whereas over 46,000 patients have taken Raptiva, only roughly 1,000 have been taking it for three years, hence the incidence of PML with Raptiva may be higher than with Tysabri (1 in 15,000). Michael Paranzino, head of the Psoriasis Cure Now of Kensington, Maryland, feels that banning Raptiva isn't warranted, especially as market leader Enbrel only relieves 50% of patients. "Before a ban, why not consider restrictions on continuous, multi-year use? Why not consider having it as a second- or third-try option if the experts are convinced there are other, first-line options that are safer?" According to senior manager at Genentech, Tara Cooper, the company is working with the FDA, possibly to develop a risk minimization plan. *Laura DeFrancesco*