

Genmab's lead cancer drug disappoints

Without Effect (this time)



Photo: wk

Its ability to combat non-Hodgkin's lymphoma might be as ephemeral as a soap bubble, but Arzerra has more to offer.

Genmab's head executive and founder, Lisa Drake-man, must digest some unpleasant results about her company's lead cancer drug, Arzerra. The fully human antibody that targets the CD20 molecule that is found on over 90% of B-cell lymphomas, didn't perform its latest task of helping patients with non-Hodgkin's lymphoma (NHL). Genmab has realised that Arzerra will possibly never be the rival drug for Genentech's/Roche's blockbuster Rituxan, another antibody to target CD20 that was approved in 1997.

The disappointing phase III trial data pushed Genmab's shares down from €28 to €18 within days (a 36% loss) and annihilated expected milestone payments from partner GlaxoSmithKline (GSK). GSK had placed a long-term €1.5 billion partnership deal for Arzerra in December

2006. Genmab now faces a full-year operating loss of about €86 million instead of a €53 million loss forecast before the Arzerra trial disaster.

Fortunately for Genmab, Arzerra is far from being a complete disaster. The antibody has proved its effectiveness in other indications and is expected to gain marketing approval for the treatment of chronic lymphocytic leukemia (CLL) this year. In addition, the drug is in clinical development (stages I, II and III) for the treatment of several more diseases, such as rheumatoid arthritis (RA) and diffuse large B-cell lymphoma (DLBCL).

After having bet a king's ransom on Arzerra, GSK has no choice but to carry on with Genmab's fully human antibody, whether the story ends up in heaven or hell.

-WK-

Resistance challenges antiviral drug concept

Doubtful Benefit

Like a deer in headlights, the world is awaiting an influenza A/H1N1 pandemic. While vaccine makers are forging ahead in developing a prophylactic serum (see related story), increasing resistance to Roche's antiviral drug Tamiflu is worrying the health authorities. According to the World Health Organization (WHO), in August Tamiflu-resistant viruses were sporadically found in several Asian countries, such as China, Singapore and Japan. Until now Tamiflu (and the related Glaxo drug Relenza) have been, next to vaccines, the second arrow in physicians' quiver against influenza A/H1N1.

Genetic sequencing business

Next Next Generation

The "big three" in sequencing, Illumina, Roche/454 and Applied Biosystems, should prepare themselves for a rough ride. A small private company from Menlo Park, California, called Pacific Biosciences (PacBio), is going to overthrow the world of genomic sequencing (and to make all shiny "next generation" machines redundant). In August, Pacific raised an equivalent of another €48 million in financing to proceed in developing its promising SMRTM (single molecule real time) sequencing system. The new investors include the US agricultural biotech kraken Monsanto and the UK's Wellcome Trust. In the recent twelve months, the shaky startup has raised an equivalent of impressive €133 million altogether.

According to Pacific, the tongue twisting SMRTM technology, developed at Cornell University (Ithaca, NY) in the last ten years, will be able to sequence a genome in five to 30 minutes. Current companies' devices, such as Illumina's Genome Analyzer II, require a whole week for the same task. The SMRTM concept is the brainchild of Cornell's applied physics professor Watt Webb (a pioneer in fluorescence correlation spectroscopy, FCS, and multiphoton microscopy, MPM) and his colleague Harold Craighead (an expert in ultra-small structures and devices). Both are on Pacific Biosciences' scientific advisory board, by the way, as well as Nobel laureate Roger Kornberg, and have a share in the company.

A former staff member of Craighead's project team at Cornell which developed the technology now employed by Pacific Biosciences, is Stephen Turner. (see photo). Turner, who was co-author of a 2003 cover story in *Science* that introduced SMRTM to the



Stephen Turner,
Pacific Biosciences

scientific community, founded Pacific Biosciences (formerly Nanofluidics) in 2004 and is now the company's Chief Technology Officer.

Pacific Biosciences intends to launch the commercial version of SMRTM in the second half of 2010. Provided that the cost is really "far lower than today's products" (as claimed by Pacific), the extreme speed of the technology has the potential to become the new gold standard for genetic analysis and completely revolutionise biomedical research. Some even say that it could "help scientists to realize the potential of personalized medicine".

Well, something along those lines was always anticipated for the current "next generation" machines, too. However, there are still no signs of a medical revolution. Time will tell if Pacific's next next generation gadgets can get one started.

-WK-

Is an increasing resistance to Tamiflu really so worrying? Not really, in the light of the still unclear benefit of the antiviral drug. Tamiflu's active agent Oseltamivir blocks the activity of the viral enzyme neuraminidase (which cleaves the glycosidic linkages of neuraminic acids) and thus, theoretically, prevents new viral particles from being released by infected cells. In practice, however, Tamiflu shortens the duration of illness for an average of just one day (from eight to seven days) and alleviates symptoms. While the WHO suspects that the drug is able to reduce influenza mortality, there is no clear evidence for this.

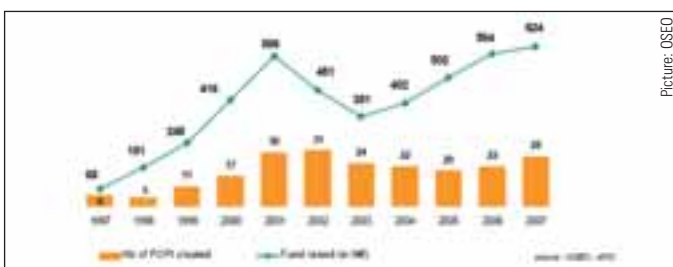
More worrying, however, is another aspect of Tamiflu resistance. Has the pandemic influenza A/H1N1 virus subtype already swapped genes with the seasonal H1N1 virus? Instructed by the WHO, laboratories worldwide are looking for genetic reassortments in the pandemic virus. So far, they haven't found any. -WK-

European cross-border investment

Fortunes to be found in Germany?

Prize question: In companies of which kind will France's tax-advantaged early-stage investment funds (FCPIs) invest their money in the future? Answer: In German companies.

After having scattered seeds in their country of origin since 1997, France's busy seed financing scene is looking to eastern markets, according to an analysis on *ScienceBusiness.net*. FCPI management companies such as AGF Private Equity, OTC Asset Management and Credit Agricole Private Equity (CAPE) have shaken up the funding scene in the recent ten years, attested financial expert Wolfgang Krause to *ScienceBusiness*, "one can hardly imagine the French venture capital market now without the FCPIs." According to the French government innovation agency, OSEO, between 1997 and 2007 over 2,500 investments were made by FCPI funds, raising about €4.4 billion (see picture).



Effective French model: The number of FCPI created (yellow) and the fund raised (green; in M€) between 1997 and 2007.

Characteristics of the "French model" also known as FCPI, are, amongst others, a tax break on 25% of the investment, as well as a capital gain exemption if shares are held for at least five years. German biotech firms demanded a similar model for a long time without success, saying that the current support of seed stage firms by the High Tech Gründerfond and KfW is not sufficient.

Increasingly, however, the French market is overgrazed, tempting French investors to look for interesting start-ups in neighbouring countries. Several of them have already opened offices in Germany. Given the fact that annual VC investment in Germany is about half of that in France, there should be countless interesting investment opportunities coming up. -WK-

Swine flu vaccine

Clinical Trials to Start Soon



The first clinical trial of a vaccine against the pandemic (H1N1) 2009 influenza virus will be conducted in Germany from August. Within a few weeks, the drug manufacturer GlaxoSmithKline (GSK) hopes to be able to assess the use of the vaccine in 128 healthy adults. According to Thomas Breuer, Chief Medical Officer of GSK Biologicals, the next step is to start 16 additional clinical trials of GSK's pandemic vaccine in over 9,000 individuals across Europe, Canada and the US, covering infants, children, adults and the elderly. The new vaccine comprises antigen components of the pandemic influenza A/H1N1 2009 strain, together with GSK's adjuvant system AS03. It is given as two doses, 21 days apart. -WK-