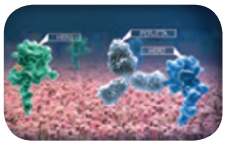
IN brief

FDA approves pertuzumab



The highly anticipated US Food and Drug Administration's approval on June 8 of Perjeta (pertuzumab) for metastatic HER2/neu-overexpressing breast cancer provides additional benefit to a patient population who, before the advent of the first HER2-directed therapy in 1998, generally had a poor prognosis. The agency approved Genentech's monoclonal antibody to be used in combination with Herceptin (trastuzumab) and Taxotere (docetaxel). Perjeta is a HER-dimerization inhibitor that hits a different epitope on the HER2 receptor than that targeted by Herceptin, and the combination of the two has an additive effect. In the phase 3 Cleopatra trial that led to the approval, women who received the Perjeta-Herceptin-Taxotere combination achieved a 6.1-month improvement in progression-free survival (PFS) over those in the control group receiving Herceptin and Taxotere plus placebo. (In absolute terms, those in the treatment arm attained a median PFS of 18.5 months versus 12.4 months for those in the placebo group.) Overall survival data are expected in 2013, but the PFS data were sufficiently strong to convince the FDA of the drug's efficacy, despite agency concerns that manufacturing problems at the S. San Francisco–based Genentech could limit its initial availability. Perjeta is still undergoing regulatory review in Europe. A subsidiary of Basel-based Roche, Genentech, which developed the two drugs, also recently reported that T-DM1 (trastuzumab emtansine) led to better PFS than a combination of the HER2 signal inhibitor Tykerb (lapatinib) plus Xeloda (capecitabine) in a pivotal phase 3 trial in metastatic breast cancer patients who had relapsed on Herceptin. "You're now getting multiple ways of targeting one key oncogene," says Susan Cleator, an oncologist at Imperial College NHS Healthcare Trust London. "Pertuzumab and the other drugs that are coming after it are opening up the possibility of treating HER2$^+$ breast cancer with biologic therapy alone, without chemotherapy." Such an approach could alleviate the long-term toxicity risks associated with chemotherapy, which include secondary malignancies and impairments of cardiac and ovarian function. Figuring out the optimal treatment regimens for different categories of HER2$^+$ breast cancer patients may be hampered, however, by a lack of biomarkers and by the very success of the drugs themselves. "Because we're currently curing so many people, the event rate is lower than it's ever been," says Justin Stebbing, professor of cancer medicine and oncology at Imperial College. *Cormac Sheridan*

On May 15, Merck KGaA announced details of its cost-cutting plans, promising shareholders that after absorbing restructuring costs of €600 ($750) million there would be savings of €120 ($150) million per annum from closing the R&D hub in Geneva.

Even for a city as prosperous as Geneva this is a large chunk of cash to be fleeing the local economy. Oschmann says Merck KGaA will soften the blow by "exploring potential entrepreneur partnership programs and redeployment proposals," and will commit up to €30 ($37.5) million in seed funding for programs that it decides to divest.

When Merck KGaA confirmed on June 19, after a consultation period with employees, that the closure was going ahead, Francois Naef, chairman of the board of Merck Serono, said, "we have already received many proposals [to spin-out programs] and several are at an advanced stage of discussion."

Supporting this are the Geneva-based Eclosion bioincubator and the venture capital firm Index Ventures, which have set up a working group to assist projects spun out of Merck Serono. "This initiative is about solidarity, there is no wish to get anything from it for Index," said Michèle Ollier, partner at Index. Hard though the closure is, she believes it could set off a wave of innovation. "The way to make something good come out of this is to team up and help with the startup of new companies. This will help create a more entrepreneurial culture," Ollier says.

The working group is also busy identifying job vacancies in the area. With so many people being laid off, it is unlikely they can all be absorbed. However, Ursula Ney, CEO of one small biotech, GenKyoTex of Geneva, says this is an opportunity for the anti-oxidative drugs specialist as it moves toward clinical development. "We are looking to do a small amount of recruitment now, and we have had approaches from people working at Merck Serono, so that's a positive side."

For Martin-Garcia, what is needed now is for the European biotech sector to be reformatted to reflect the new reality of the industry, which is that pharma is intent on defraying risk by outsourcing early-stage research. "SMEs [small-to-medium sized enterprises] and specialty biotechs need to do early-stage development of assets that can be partnered. The quality of European science plays into that, but it will be a hard transition," he comments. **Nuala Moran** *London*

Box 1 One of Europe's elite

Beyond its significance for Geneva and for Switzerland, Merck Serono's closure is a heavy loss for the European biotech sector. Serono's roots in biopharmaceuticals go right back to the start of modern biotech, when it succeeded in manufacturing recombinant versions of human proteins in mammalian cell lines. The company can claim credit for the world's first human birth in 1992 from a recombinant fertility treatment, the first approval for recombinant human growth hormone as a treatment for AIDS wasting and the recipient of a European Orphan Drug designation. Serono was also an early exponent of biotech deal making, acquiring the human fertility division of Integrated Genetics Laboratories from Genzyme in 1989, as the basis of its world-leading franchise in recombinant human fertility hormones.

In its heyday, Serono had three products approved by the US Food and Drug Administration within six weeks. Between August and October 1996, the company received the nod for Serostim, human growth hormone for treating AIDS wasting; Saizen, growth hormone for treating short stature in children; and the recombinant follicle-stimulating hormone Fertinex. It was the US launch of its recombinant interferon beta-1a product Rebif for multiple sclerosis in 2002, however, that put Serono on the path to blockbuster status. Worldwide Rebif sales reached $813.8 million in its first full year and by 2004 sales had broken the $1 billion barrier.

From 2002, however, the once-productive pipeline started to splutter. In May of that year, Rebif failed in a phase 2a trial in rheumatoid arthritis, and a plan to develop an inhaled version of the product came to nothing. Attempts to diversify the portfolio also came unstuck, with the failure of a phase 3 cancer vaccine and a phase 3 psoriasis treatment. In 2005, some of the shine also came off the US franchise when Serono was forced to pay $704 million in fines as part of a guilty plea to charges including Medicaid fraud and marketing conspiracy.

In the face of these setbacks, the Bertarelli family, as majority owner (with 62% of the equity), exercised its prerogative and at the end of 2005 put Serono up for sale for the asking price of $15 billion. In September 2006, he agreed to sell the company to Merck KGaA for $13.3 billion. **Nuala Moran** *London*

© 2012 Nature America, Inc. All rights reserved.
npg