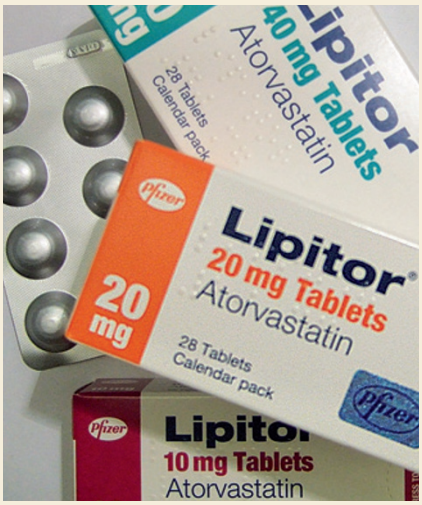
NEWS IN BRIEF

End of the Lipitor era



Pfizer's atorvastatin (Lipitor) — which cumulatively grossed over US$130 billion in sales since its approval in 1996 — came off patent on 30 November.

The lowdown: Atorvastatin was first synthesized in 1985 by Bruce Roth, who at the time was working at Warner-Lambert. The statin faced a heavy uphill battle, because the first-in-class hydroxymethylglutaryl CoA reductase inhibitor, Merck and Co.'s lovastatin, was already in late-stage trials when atorvastatin was synthesized. However, when a first trial of atorvastatin in humans — carried out on 24 Warner-Lambert employees — suggested high efficacy, the company decided to advance the project against the odds.

Atorvastatin was eventually approved by the US Food and Drug Administration in 1996 as an adjunct to diet to reduce levels of 'bad' low-density lipoprotein (LDL) cholesterol in patients with hypercholesterolaemia. It was the fifth statin to make it to market in the United States, following lovastatin, simvastatin, pravastatin and fluvastatin. To tackle the considerable competition, Warner-Lambert partnered with Pfizer, then the fifth biggest pharmaceutical firm, to co-market the drug. Relying heavily on atorvastatin's relatively high potency, the late-comer quickly moved up the pack. After post-marketing studies drove home the value of aggressive LDL cholesterol lowering in patients with coronary heart disease as a means of reducing the risk of cardiovascular events, and statin use became more widespread, sales of the drug went through the roof. In 2010, sales of the drug were $10.7 billion, down from a peak of $12.9 billion in 2006.

The drug's success led to Pfizer's $90 billion acquisition of Warner-Lambert in 2000, after a bidding war with American Home Products — still one of the biggest acquisitions in US history. American Home Products renamed itself Wyeth in 2002 and was acquired by Pfizer in 2009, as Pfizer looked for strategies to counteract the huge loss of sales once the patents on atorvastatin expired.

The statin came off patent in the United States on 30 November, and is due to come off patent in most European countries in May 2012. Pfizer has aggressive plans to maintain market share, but the company is still expected to take a large hit on the patent cliff. Barclays Capital analysts have forecast an 87% reduction in atorvastatin sales in the United States for 2012.

Moving towards quantitative and systems pharmacology

The NIH has released a white paper on the value of 'Quantitative and Systems Pharmacology', even as universities start stepping up to the challenge.

The lowdown: A 48-page report for the US National Institutes of Health (NIH) has called for the development of Quantitative and Systems Pharmacology (QSP), a merger of systems biology and pharmacology that aims to develop and combine mathematical, computational and experimental methods towards understanding how drugs modulate cellular networks in space and time.

The report — co-chaired by Harvard's Peter Sorger and Merck's Sandra Allerheiligen, and written following two NIH workshops that brought together academia, industry and government — argues that by fostering the emerging science, the NIH can help to tackle industry problems including target assessment and an inability to predict the therapeutic and toxic effects of drug candidates in humans. Specific research foci that the report recommends include the need to: characterize the networks in which drug targets are embedded; investigate the origins of variability in drug response at the single-cell, organ and patient level; and develop approaches to understand why drugs fail in clinical trials. "[QSP] will … become a core discipline of translational medicine," write the authors.

"White papers are usually intended to be the first step towards a major funding initiative from the NIH," says Marc Kirschner, Chairman of Harvard Medical School's Department of Systems Biology. Kirschner, Sorger and colleagues recently launched the Initiative in Systems Pharmacology at Harvard, with goals that are in line with the white paper's recommendations (see page 894). The University of California San Francisco, USA, similarly inaugurated its Center for Quantitative Pharmacology in September.

AstraZeneca/Targacept's antidepressant fails in first Phase III trial

The first of four pivotal trials of AstraZeneca/Targacept's TC-5214 for major depressive disorder has failed.

The lowdown: TC-5214, the S-enantiomer of the antihypertensive agent mecamylamine, is a nicotinic channel blocker that was patented at the University of South Florida, USA, and subsequently licensed to Targacept. In 2009, after a Phase II trial run in India suggested that the drug was a highly effective antidepressant, AstraZeneca paid $200 million upfront and pledged another $1 billion in milestones for co-development and commercialization rights to the drug.

The first Phase III data from the drug question the wisdom of the investment. RENAISSANCE 3 randomized 295 patients with major depressive disorder to treatment with either TC-5214 or placebo, as an adjunct to selective serotonin reuptake inhibitor or serotonin–noradrenaline reuptake inhibitor background therapy. Treatment did not perform better than placebo on the primary end point — change on the Montgomery–Asberg Depression Rating Scale after 8 weeks — say the sponsors. The drug's adverse event profile was consistent with the earlier Phase IIb study.

Results from three more ongoing Phase III trials of TC-5214 are due over the next 6 months, and the partners plan to disclose detailed trial results from RENAISSANCE 3 only after these have been completed. In the meantime, the partners are still working towards filing the drug in the United States in the second half of 2012.