

IN brief



Amylin's diabetes shock

In a major setback for Amylin, the US Food and Drug Administration called for

Fears over long QT.

further tests on Amylin's Bydureon, a once-weekly drug for type 2 diabetes. On October 19, the San Diego-based biotech Amylin, and partner Eli Lilly of Indianapolis, announced that the agency had issued a Complete Response Letter calling for a study known as thorough QT to further investigate the potential effect of the drug's cardiac effects. Bydureon is a long-acting formulation of Amylin's approved drug Byetta (exenatide), an analog of the insulin-boosting glucagon-like peptide 1 (GLP-1) (*Nat. Biotechnol.* **28**, 109, 2010). Both contain exenatide, but Bydureon contains a higher concentration of the active agent, delivered into the blood by controlled release. The first-in-class synthetic gut hormone drug Byetta generated \$677 million in 2009 in the US alone. But Bydureon's formulation—once weekly injections compared with twice a day—is predicted to gain competitive edge over its predecessor if approved. Simos Simeonidis, managing director and senior biotech analyst at Rodman & Renshaw in New York, says that Bydureon had “blockbuster” potential and could have brought in at least \$1 billion per year for Amylin after the first few years. The FDA's concerns over supratherapeutic concentrations of exenatide may have been triggered by observations in a Byetta study, in which a few patients with blood levels of 500 pg/ml had lengthened QT intervals. In patients with kidney problems, once-weekly Bydureon can reach five times the normal 200 pg/ml seen with Byetta. Given the delay in approving Bydureon, alternate treatments for type 2 diabetes like Victoza (liraglutide) from Novo Nordisk, of Princeton, New Jersey, and Amylin's own Byetta, are now expected to flourish. London-based GlaxoSmithKline's investigational Syncrion(R) (albiglutide), also a GLP-1 analog, is currently undergoing phase 3 clinical trials. “They were considerably behind,” says Yaron Werber, senior biotech analyst at Citigroup in New York. “But now I think they have a chance to close a big part of the gap.”

Nidhi Subbaraman

IN their words

“At this juncture, I don't know that individuals will have all that much to gain from publishing their data, but I think that Genomes Unzipped will help to prove that there's not all that much to lose, either.” Linda Avey, cofounder of 23andMe, comments on a move by 11 British-based scientists and a US lawyer to make their own genetic tests publicly available in the hope of encouraging others to share their genome information. (*The Times*, 11 October 2010)

Table 1 Vaccine mergers & acquisitions

Acquirer	Target (location)	Value	Year
Berna Biotech	Rhein Biotech	\$257 million	2002
Crucell	Berna Biotech	\$449 million	2005
Crucell	SBL Vaccin	\$52 million	2006
GlaxoSmithKline	ID Biomedical (Vancouver, Canada)	\$1.4 billion	2005
GlaxoSmithKline	Corixa (Seattle)	\$300 million	2005
Intercell	Iomai (Gaithersburg, Maryland)	\$189 million	2008
Novartis	Chiron (Emeryville, California)	\$5.4 billion ^a	2005
Sanofi Pasteur	Acambis	\$549 million	2008
Sanofi Pasteur	Shantha Biotechnics	\$781 million ^b	2009
Sanofi Pasteur	VaxDesign (Orlando, Florida)	\$55 million ^c	2010

^aThe transaction involved the remaining 58% of Chiron's stock not already held by Novartis. ^bTotal valuation of the company implied by the terms of the deal. Sanofi Pasteur acquired an 80% stake. ^cThe deal includes \$5 million in potential milestone payments.

unit, just as it has with several earlier acquisitions, such as antiviral drug developer Tibotec of Antwerp, Belgium, and antibody developer Centocor located in Horsham, Pennsylvania.

J&J's imminent acquisition of Crucell is further evidence that the vaccines area, although small in the context of overall pharma sales, is firmly back on the industry's agenda, after a couple of decades during which it had fallen out of favor. Other acquisitions where vaccines have featured prominently (though not exclusively) are Pfizer's takeover of Wyeth and London-based AstraZeneca's \$15.2 billion acquisition of Gaithersburg, Maryland-based MedImmune.

The vaccines market's steady growth equilibrium is punctuated by irregular spurts caused by significant new product introductions. For instance, Wyeth's Prevnar (pneumococcal 7-valent conjugate) or Gardasil (human papillomavirus quadrivalent (types 6, 11, 16 and 18) recombinant vaccine) from Merck of Whitehouse Station, New Jersey, quickly added substantial chunks of revenue to the industry total.

The complexities of manufacturing, combined with the economies of large-scale production, have conspired to make the sector strongly oligopolistic, with the market dominated by a small number of firms. The top five players, Sanofi Pasteur, GSK Biologicals, Merck, Pfizer and Novartis, control around 85% of the market, with around \$18 billion of sales in 2009, according to market analysts VacZine Analytics, of Bishop's Stortford, UK. “The industry last year grew by about 9, 10% over the previous year,” says VacZine Analytics director John Savopoulos. By his reckoning Crucell's 2009 vaccine sales of €304 million (\$424.3 million) would rank the company in ninth place, behind CSL, of Parkville, Australia, and London-based AstraZeneca's MedImmune unit. The H1N1 influenza pandemic had the biggest impact on sales in 2009, bringing in around \$3.5 billion in additional revenue. In the first three-quarters of 2010, the top five companies posted combined sales

of \$16.9 billion, excluding the contribution of Sanofi Pasteur MSD, a European joint venture between Sanofi Pasteur and Merck.

Nevertheless, the industry's pipeline remains widely distributed. “Seventy companies are now targeting 40 plus pathogens,” Savopoulos says. Some 160 vaccines are in clinical development, around 100 of which are in phase 1 trials. Crucell has the industry's fifth largest pipeline, he notes. It has clinical-stage programs in yellow fever, tuberculosis (TB), malaria, HIV, Ebola virus and Marburg virus as well as preclinical efforts in seasonal influenza, respiratory syncytial virus and in the development of a universal flu vaccine. Only GSK Biologicals, Sanofi Pasteur, Novartis and Merck have more vaccine programs in the clinic. “They look reasonably well positioned. The problem is when you probability-adjust their pipeline—malaria, TB—they're tough areas to be in,” Savopoulos says. A pre-clinical antibody development program, which targets both seasonal and pandemic flu strains, and has attracted \$40.7 million in US National Institutes' of Health funding (with potentially \$28.4 million more to come), was the main focus of J&J's 2009 alliance with Crucell. “That technology, if it can be harnessed for an active vaccine, that's a quantum leap above the existing flu market,” Savopoulos points out. Jan Van den Bossche identifies a combination monoclonal antibody development program for treating individuals exposed to rabies infection as particularly promising. “It's a clear, understandable program,” he says. The program, in phase 2 trials, aims to replace an existing equine immunoglobulin therapy.

Although J&J will seek further growth from Crucell's existing product portfolio, J&J's real measure of success will be in the extent to which it can convert pipeline promise into commercial reality. Sanofi Pasteur 'turbocharged' Acambis's ChimeriVax platform when it acquired the Cambridge, UK-based firm, says Savopoulos. “The question is, can J&J do the same thing?”

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