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Cantab failure shows need for wide portfolio

The failure in mid-October of Cantab's (Cambridge, UK) lead vaccine TH-GW for the treatment of genital warts knocked more than two-thirds off the company's share price, forcing the resignation of CEO Jurek Sikorski and leaving Cantab up for sale. During the past three months, this and other biotech product disappointments have provided a reality check for the sector, highlighting the need for companies to spread their risk over a broad product portfolio—even if it means consolidating.

The failure of one of Cantab's most advanced vaccines in phase II was "a big surprise and a big disappointment," according to vice president of investor and media relations Andrew Burrows. Previously, phase II trials had shown that the vaccine—a subunit of human papillomavirus 6 with an alum adjuvant—had "great immunogenicity," and analysts had predicted peak sales of around $400 million. However, in two subsequent phase II trials, carried out by Cantab's collaborator SmithKline Beecham Biologicals (Rixensart, Belgium), TH-GW was no more effective than placebo. SmithKline dropped the program and Cantab's share price plummeted to 76p, reducing the market value of the 11-year-old company to around £33 million ($46 million). Shares in Cantab had peaked in March this year at more than 700p.

Burrows says that the market's response to the news of the product failure has been an "over reaction," pointing out that Cantab has six other vaccines in clinical development. Moreover, only one vaccine, TA-CIN, a human papillomavirus-based vaccine for the treatment of cervical dysplasia, uses similar technology to that of the failed vaccine. "Investors are often not sophisticated enough to make this distinction," says Burrows.

Nevertheless, Cantab is now up for sale, although Burrows says that the company is not in a desperate situation. Analysts agree that Cantab, which has strong intellectual property in therapeutic vaccine development and employs well-respected vaccine experts, could get a good price. And indeed, rumours that there had been a number of interested parties sent Cantab's share price shooting back up to around 140p. Moreover, the company has £20 million in cash (enough for about 2 years), which would be an attractive bonus. However, Ian Smith, biotechnology analyst at Lehmann Brothers (London), says that the potential value of the company now rests on the success of its DISC HSV vaccine, which is currently in phase II trials for the treatment of genital herpes under a collaboration with Glaxo Wellcome (Greenford, UK).

Cantab's vaccine has not been the only high-profile product disappointment during the past two months. In October, around 70% was written off the share price of Scotia Holdings (Stirling, UK) after it announced that the FDA has rejected its application for Foscan, a light-activated treatment for head and neck cancers; British Biotech (Oxford, UK) chalked up another clinical failure for its cancer drug, Marimastat (*Nat. Biotechnol.* 18, 1138); while in the US, shares in Cell Pathways (Horsham, PA) slid 60% after the FDA rejected its application to carry out further clinical trials of Aptosyn, an oral treatment for familial polyposis; and also in October, Connetics (Palo Alto, CA) lost almost 80% of its share price on pulling its experimental treatment for scleroderma—human recombinant relaxin—after phase III trials suggested it was ineffective.

Such failures in drug development are inevitable, and biotech companies need to be adept at limiting the damage that can result. "You can only avoid a massive hit of [negative] investor sentiment by building a broad portfolio of products and intellectual property...this then spreads the risk for investors and ensures sustainable growth," says Burrows.

However, Cantab learnt this lesson too late. Bill Blair, biotechnology analyst at Nomura International (London), says that Cantab had been looking to broaden its pipeline through acquisitions for 18–24 months. "Sikorski can't be blamed for the failure of the genital warts vaccine, but it was in his failure to consummate a deal in time." Cantab had been in talks with rival vaccine company Peptide Therapeutics (Cambridge, UK) that broke down at the end of September when the two companies failed to agree on the terms of the deal; US healthcare company Baxter (Deerfield, IL) subsequently bought 20% of Peptide.

Burrows acknowledges that the body blow suffered by Cantab passed without effect on the share price of its multinational collaborator SmithKline Beecham, which has a deeper pipeline and more secure sources of funding. "There will no doubt be companies out there who are now looking very carefully at their M&A plans," says Burrows. And Blair agrees that the climate is changing. "At least in the UK sector, talk of M&A activity is less muted than it had been in 1999."

But other companies may have already missed the boat. Scotia's future, for instance, looks bleak; it has little cash and has no other products in the clinic. Foscan may be an effective drug, but it would take time and money to prove this to the FDA—Scotia has neither. Cell Pathways could also be vulnerable to takeover: It has no other products close to market, few lucrative pharmaceutical alliances, and little in the way of cash.

However, cash—combined with collaborations or marketed products—may protect the other two, at least in the short term: Despite the repeated failure of Marimastat, British Biotech is relatively well financed with $76 million cash (enough for about 10 years), and its new management appears to be committed to turning the company around, says Blair. The company has already begun to "repackage" its expertise in metalloenzyme inhibitors, signing up Swiss biotech giant Serono (Geneva) in mid October in a research partnership focusing on inflammatory disorders. And Connetics' disappointment over relaxin may be buffered by the 5 years worth of funding it has in reserve. With two products recently launched, it can convince investors that it is still on track to profitability. "Cash is king," says Blair. But if cash is short then companies may face the inevitable prospect of being swept up in consolidation.

Liz Fletcher

HGS targets patent-expiring drugs

Human Genome Sciences (HGS; Rockville, MD) hopes to re-patent many of the biotechnology industry's most celebrated therapeutic proteins and return them to market under its own banner. It plans to do this by extending their blood circulation half-lives by fusing them with human blood serum albumin using technology it purchased in September. HGS has already filed an Investigational New Drug application with the FDA for its interferon-based hepatitis C treatment albuferon, and at least eleven more are underway. However, apart from the fact that extending half-life is not always advantageous, HGS faces competition from companies offering alternative half-life extension technologies.

HGS bought Principia Pharmaceuticals (Norristown, PA) and its albumin fusion technology using $135 million in stock. The move, which closed Principia's brief tenure of independence since being spun off from Aventis last year, ended a three-year search by HGS for a better way to extend protein half-life. Typical half-lives—lasting minutes to hours—require

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