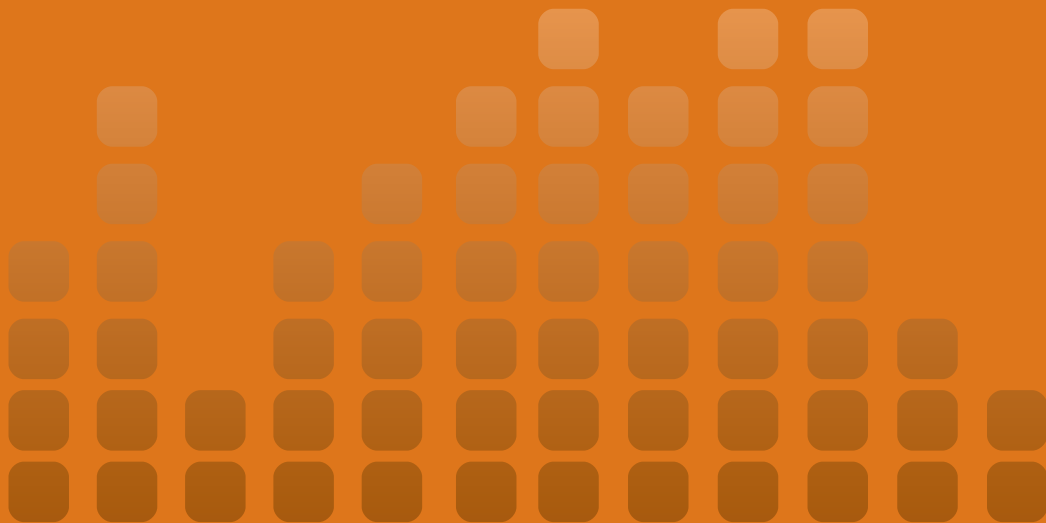


Analysis of Deal Making in Vaccines



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Trends in Deal Structures and Valuations

Dr Danya Morton-Holmes and Nick Fyson
with members of PharmaVentures Corporate Advisory

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Fuelled by pandemic flu threats and increased government funding, the market for seasonal influenza vaccines has grown rapidly since the mid-2000s, reaching almost US\$3 B in major markets in 2008/2009 and forecast to grow rapidly to more than US\$5 B in 2010/2011. The current WHO phase of pandemic alert is "Post Pandemic" reflecting a return to normal levels of seasonal influenza disease activity. However the pandemic threat can emerge at any time providing opportunities for companies who can ramp up their vaccine development and manufacturing capability at short notice. The main players in the vaccines field have the size advantage to maintain a large vaccine development and production capability even during periods when seasonal vaccines are not required in large amounts. This has created an environment where new technologies for developing and manufacturing efficacious vaccines in large quantities at short notice is a key driver for deal making in this sector.

The need for primary prevention of infectious diseases remains strong and, with other drivers such as the ongoing threat of bioterrorism, significant unmet needs in the developing world, and the prospect of treating non-infectious diseases, the lacklustre vaccine market of the 70s and 80s has been replaced by a research-intensive, fast growing sector. Although dominated by a small number of global pharma companies, the rapid uptake and commercial success of novel, high priced products such as Prevnar® and Merck's Gardasil® (for the prevention of HPV) have led to a wealth of new approaches, technologies and products being developed by smaller players. Dendreon is the success story of a new entrant entering the vaccines arena. The company, founded in 1992, is forecast to achieve revenues of over US\$3 B in 2016 from sales of its first product, Provenge®, the first autologous cellular immunotherapy approved for the treatment of prostate cancer. No doubt the bigger vaccine players would be keen to acquire such technologies for themselves increasing the attractiveness for such deals.

Vaccines are once again a focus for pharmaceutical and biotechnology companies, rather than the poor relation of traditional drug products.

1.2 Market size and trends

The vaccines market is currently dominated by five global pharma players: GlaxoSmithKline, sanofi-aventis (with its vaccines arm, Sanofi Pasteur), Pfizer (as a result of its acquisitions of Wyeth and PowderMed), Novartis (with its acquisition of Chiron) and Merck & Co. Inc. These five companies had combined vaccines sales of more than US\$18 B in 2009 out of a total market of around US\$20 B.

Johnson & Johnson (J&J) has also signalled its strategic intent to become a major player in the vaccines field with its recent move to acquire Crucell NV (Deal no. [37462](#)) for more than US\$2.4 B. This provides J&J with a vaccine platform at a

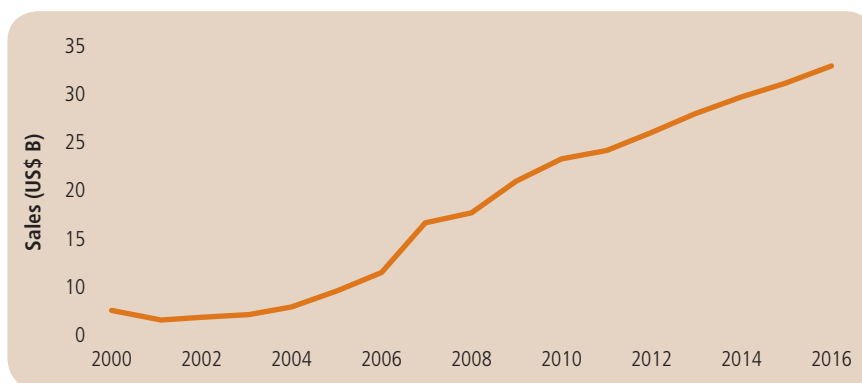


Figure 1 – Total sales of vaccines between 2000-2016 (Sales data from 2010 is a forecast). Source: EvaluatePharma®

time when the vaccines business is becoming increasingly attractive because of its relative cost-effectiveness, limited exposure to generics and growth opportunities.

This report focuses predominantly on the human vaccines industry, but there is also a thriving market in animal vaccines, valued at more than US\$4 B in 2009.

The past decade has seen rapid growth in the vaccines sector, with 21% CAGR outperforming the 8% CAGR the pharma industry as a whole has been seeing. As a consequence, vaccines are becoming increasingly important as revenue generators within the portfolios of the key pharma players. Total vaccines sales for 2016 are forecast to be over \$32 B (*Figure 1*) reflecting a CAGR of 8% between 2009-2016, still more than double the CAGR of 3.3% expected for the industry as a whole in the same period.

Although part of the revenue growth has been driven by the introduction of new products and an increase in average pricing (rather than an increase in volumes of traditional vaccine products), there are a number of other factors driving the strong growth and renewed interest in the sector, as outlined below:

Relatively limited competition

With only a handful of the global pharma players involved in the vaccines area and a wealth of potential for new products, companies faced with diminishing pipelines, increasing generic competition in their traditional core franchises and a need for innovative development strategies have come to view vaccines as a potential future driver of growth.

High barriers to entry

Complex manufacturing, large capital investments and intellectual property considerations provide high barriers to entry for new entrants but make vaccines an attractive sector for established companies.

A step change in pricing

As indicated above, with the introduction of novel vaccines in the 1990s came the opportunity for improved pricing and margins, serving to establish vaccines as a commercial opportunity on a par with traditional drug products.

Demonstration of the cost-effectiveness of vaccines

Large-scale government investment in vaccines has improved with an increased understanding of the cost-effectiveness of vaccination compared with other healthcare interventions. In numerous studies, the costs of preventative vaccination have been shown to be much lower than the costs of treating the disease itself, in terms of, for example, hospitalisation, medical treatments and the economic impact of lost working days.

New technologies

The discovery of new technologies has meant that it is now possible to manufacture vaccines more efficiently and on a larger scale, leading to more stable production and higher margins. Technology is also fuelling progress in the search for needle-free vaccine delivery systems.

Novel targets offer huge commercial potential

In addition to ongoing efforts in infectious disease targets such as HIV and MRSA, there are attractive opportunities in vaccines for non-infectious diseases such as cancer, Alzheimer's disease, multiple sclerosis etc.

Increased public awareness of infectious diseases and bioterrorism

Highly publicised outbreaks of, for example, SARS, West Nile virus, avian flu and swine flu have led to growing public fear around the impact of a true pandemic and a rush to develop vaccines to prevent a potentially high death toll. Hospital-acquired infections such as MRSA and *C. difficile* are also the subject of research in the area. In addition, fears around biological warfare have driven governments and military organisations to fund the development of vaccines against agents likely to be used in bioterrorism.

Global travel

The general public is travelling more often and further afield leading to a higher incidence of "travellers' diseases" and an ongoing need for vaccination against diseases such as yellow fever, Hepatitis A, rabies, Japanese encephalitis, tuberculosis, malaria and typhoid fever.

Analysis of vaccines deals by deal type

A wide variety of deal types are used in the pharmaceutical arena. For the purposes of this analysis, the deal groupings include the following as taken from the PharmaDeals® v4 database:

- **Collaborative/Licensing**
Collaborative R&D, Licensing, Rights, Clinical & Commercial, Clinical co-development
- **Marketing**
Marketing, Co-Promotion, Co-Marketing, Distribution
- **Finance**
Funding, Milestones, Royalties, Equity Investment, Equity Reacquisition
- **Mergers & Acquisition**
Asset/Business/Product Acquisition, Merger, Demerger, Divestment
- **Manufacture**
Manufacture/Supply, Contract Manufacture
- **Other**
Joint Venture, Research, Evaluation.

3.1 Number of deals

Figure 13 shows the number of vaccine deals by deal type between 1996 and June 2010.

The vaccines area has been dominated by Collaborative/Licensing deals. Over the last fifteen years there have been 620 of these deals, accounting for more than a third (33.6%) of all deals in the space. The next three deal types: Finance, Technology Access and Manufacture collectively account for a further 46.5%.

The dominance of Collaborative/Licensing type deals reflects both the profile of companies competing in the vaccines space and the research intensity of the therapeutic area. New technologies and approaches are often developed initially by smaller companies and/or academic groups which then partner with larger companies to progress the project beyond early stage development to

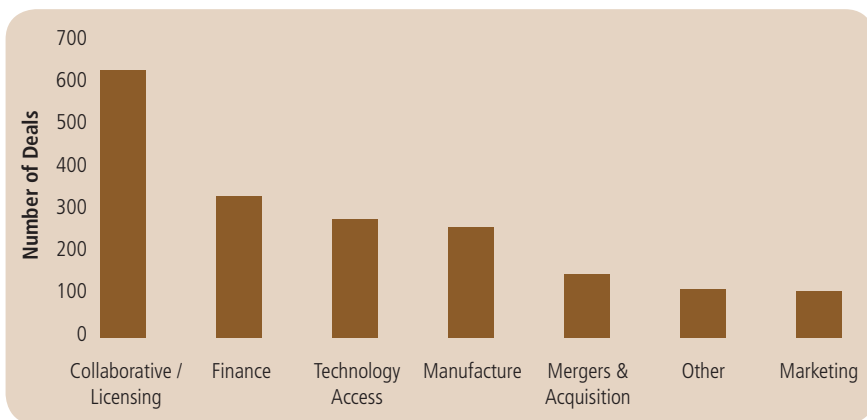


Figure 13 – Total vaccine deals by deal type (1996 to June 2010)³.

commercialisation. These smaller players rely on collaborative or licensing deals to fund their early stage research, or may also need to raise finance, as is reflected by this type of deal being the second most common in the vaccines area. In Finance deals, charities and government/military organisations have been an important source of funding for vaccines development.

3.2 Year on year analysis of vaccines deals by deal type

Figure 14 shows the breakdown of deal types year on year.

The ongoing dominance of Collaborative/Licensing type deals over the period of analysis is highlighted, reflecting the number of smaller players competing in the vaccines area.

The high number of Manufacturing collaborations and Technology Access deals is also shown. Manufacturing quality, speed and costs are clearly key hurdles in vaccine commercialisation. In terms of Technology Access, the emergence of new technologies to address the development of, for example, therapeutic vaccines

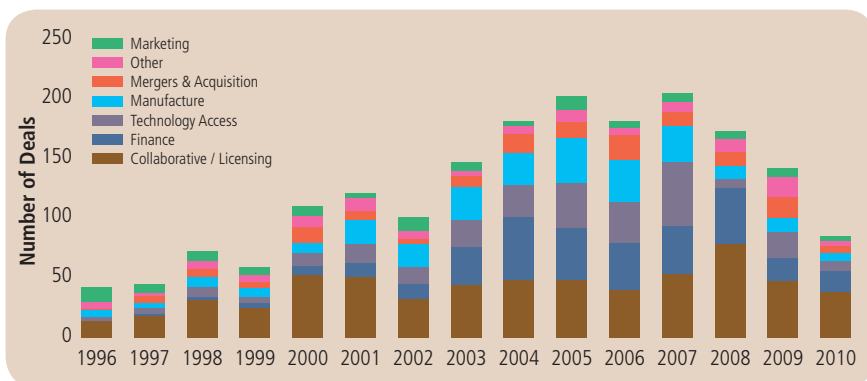


Figure 14 – Year on year analysis by deal type (1996 to June 2010).

³ Finance figures do not include venture capitalist funding

10.1

Intercell AG and GSK

At a glance

Deal number:	<u>34317</u>
Date of deal:	December 2009
Originator(s):	Intercell AG
Partnering:	GlaxoSmithKline
Deal overview:	Strategic alliance between Intercell and GSK to develop and commercialise needle-free patch-based vaccines
Total deal value (US\$ M):	173.2
Deal value detail (US\$ M):	Upfront: 49.48 Equity investment: 123.71

Details of the deal

Adapted in part from: Intercell and GSK in Alliance for Novel Patch Vaccines, *PharmaDeals Review*, Vol 2009 Issue 12, Published: 21 Dec-2009.

Summary: In December 2009, GlaxoSmithKline (GSK) Biologicals SA and Austrian vaccine maker Intercell announced an agreement for a strategic alliance to develop and commercialise innovative needle-free patch-based vaccines.

An estimated 20 million international travellers develop traveller's diarrhoea (TD) while visiting endemic areas in developing countries. Currently, there is no vaccine available to address this medical need. GSK Biologicals SA and Austrian vaccine developer, Intercell, have entered into a strategic alliance to collaborate on a TD vaccine patch and an investigational single application pandemic influenza vaccine (Deal no. 34317). GSK also has the right to use the patch technology for other vaccines in its portfolio.

Under the agreement, GSK will make upfront cash payment of €33.6 M (US\$49.4 M) along with an additional equity investment of €84 M (US\$123.5 M) through a staggered share purchase option of up to 5% in Intercell. Included in the agreement are Intercell's investigational TD vaccines currently in Phase III trials, an

investigational single application pandemic influenza vaccine in Phase II and other potential future patch vaccines.

Intercell specialises in the development of smart vaccines which stimulate both the important elements of human immune system, i.e. T- and B-cells. The vaccine against TD is easily administered through a patch placed on the skin and avoids needles. If approved, it will be the first of its kind to reach the market.

At the time of the deal, the spread of H1N1 (“swine”) flu virus had grabbed the attention of vaccine makers. GSK and Intercell will also develop a flu vaccine using the patch technology. Although the patch may take about a decade to be developed, the expected revenue is forecast to be more than US\$1 B. The current partnership will combine the strengths of Intercell’s smart vaccines with GSK’s power in development and commercialisation.

GSK intends to pursue a series of vaccine ventures in emerging markets, which currently account for 13% of its sales, to cash in on the rising wealth of these economies, through a policy of branded generics, vaccines and traditional patented medicines.

Intercell has earlier signed deals with four vaccine makers: Novartis, Pfizer, Merck, and Sanofi Aventis. GSK, the fifth in line is also the second strategic investor in Intercell after Novartis, which has a 15% stake (Deal nos. [27657](#) and [24492](#)). The current deal has come three months after Johnson & Johnson entered the vaccine space by acquiring an 18% stake in Crucell, the Dutch vaccine maker (Deal no. [33908](#)).

GSK already has about 22% of the global vaccine market in its grasp. By combining the new partner’s innovative vaccine programme technology it can look forward to significant sales in the future. As the vaccine market is attractive, Intercell believes that the diarrhoea vaccine could potentially generate revenues of US\$500 M. The company plans to conclude clinical tests in 2012 and bring the vaccine to market by 2013.

Analysts were impressed with the GSK deal, as it had a sizeable upfront and equity stake. With its successful standing in vaccines and over the counter business, Intercell is the right choice and it also emphasises the confidence in the latter’s vaccine platform. Intercell benefits on two fronts: cash injection into its R&D and access to the commercial strength of GSK. Intercell has also clearly signalled that it wants to pursue its business strategy of being an independent entity as it is confident about the potential success of its patch technology.