

An Assessment of Six Months of Drug Delivery Deal Making

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Kate Atherton joined PharmaVentures in 2005 as Publishing Editor and is a regular contributor to *PharmaDeals® Review*. Prior to 2005, Kate authored numerous articles on the subject of archaeology for academic journals and reports and recently co-authored a published monograph on a medieval moated manor house.

Introduction

During the last six months (May to October 2006), a total of 107 deals related to drug delivery have been recorded in PharmaDeals® Agreements. Although this figure is lower than that for the same period last year, when 144 transactions were recorded, the types of deal that have been made, and the types of technologies and platforms that have been the subject of these deals, indicate that drug delivery companies continue to play a vital role in the development and production of novel and innovative products. These products, and their associated technologies, have the potential to deliver both new and pre-existing drugs to far greater sections of the population, for whom these drugs may previously have been entirely unsuitable.

This article draws on deal information contained within PharmaVentures' PharmaDeals® Agreements management tool to reflect on six months of drug delivery deal making. The PDA number refers to the deal number in PharmaDeals® Agreements.

Deal Makers

A full 89% (95 deals in total) of all drug delivery deals from this six-month period featured start-up and emerging companies (*Figure 1*). Global companies, by contrast, participated in only eight deals: **Pfizer**, **GlaxoSmithKline** (GSK), **Novartis** (in two deals, one with fellow global **Schering-Plough**); **F. Hoffman-La Roche**, **Abbott Laboratories**, **Takeda Pharmaceutical** and **Merck & Co.**

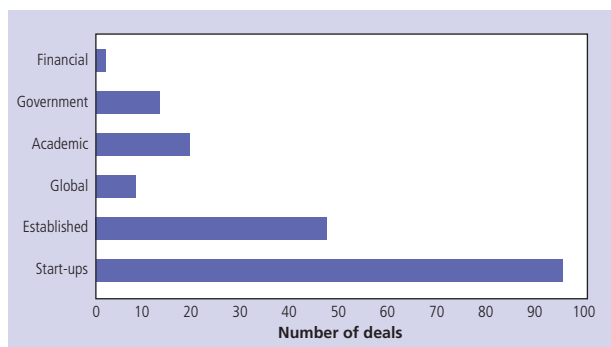


Figure 1 – The number of deals featuring each company type, May to October 2006 (Source: PharmaDeals® ©PharmaVentures).

Not surprisingly, five of these deals featured a collaborative and co-development element while licensing and technology access agreements and a business acquisition comprised the remaining three deals (see *Key Global Deals* below).

Academic institutions and government bodies participated in 22 drug delivery deals between May and October, primarily in order to aid the research and development of efficient and convenient methods of drug delivery in order to combat diseases and other medical threats that can affect large numbers of the population.

Five drug delivery deals had a potential financial value in excess of US\$50 M: the most valuable of these was between **RVX Therapeutics** and **Medtronic** (PDA no. 24807). In a deal potentially worth US\$291 M, RVX granted to Medtronic exclusive worldwide rights to develop and commercialise its ReVas™ technology for the local non-systemic treatment of cardiovascular disease.

Key Global Deals

Pfizer's acquisition of UK-based **PowderMed** represented a change in direction for Pfizer, giving it access to a promising technology that delivers DNA directly to the cells of the body's immune system and has the potential to lead to a range of new vaccines for influenza and chronic viral diseases (PDA no. 25502). In a press release, Pfizer's chief executive officer, Jeffrey B Kindler, announced that: "This acquisition is a strategic opportunity to enter the vaccine market and is part of our focus on broadening healthcare solutions for patients." The significance of this acquisition to the future of Pfizer was also apparent in the accompanying statement of the company's vice chairman, David Sedlarz: "This acquisition is an example of the fresh approach Pfizer is taking to business development... With PowderMed's novel DNA technology and its portfolio of early-stage vaccine candidates, we are adding high-potential, externally sourced product candidates and technologies to our research and development portfolio."

While this transaction may prove significant for Pfizer's future interests, it also highlights a possible leap forward for needle-free delivery systems. PowderMed's vaccine development program is based on its Particle Mediated Epidermal Delivery (PMED) technology, a needle-free

delivery system that delivers DNA-coated microscopic gold particles into the skin using pressurized helium gas. The particles penetrate the epidermal layer of the skin activating cells that in turn trigger an immune response. The vaccines, which have potential advantages over egg-based vaccines, can also be stored at room temperature and the system is sufficiently user-friendly that self-administration may be possible.

Global companies Schering-Plough and Novartis entered into an agreement on 14 August to combine two of their products to form a single inhalation device for the treatment of asthma and chronic obstructive pulmonary disease (COPD) (PDA no. 25006). The product will combine Schering-Plough's once daily inhaled corticosteroid mometasone and Novartis' once daily beta2-agonist indacaterol, potentially eradicating the need for asthma and COPD patients to use more than one treatment. The combination of corticosteroids and long-acting beta2-agonists is, according to the associated press release, 'the fastest-growing segment of the worldwide asthma market' for this very reason. It is hoped that the product will be used with, amongst other inhalers, Schering-Plough's Twisthaler® delivery device, which is an inhalation-driven device that operates with a propellant, removing the need for hand-breath coordination.

Academic Institutions

Academic institutions entered into 19 deals between May and October 2006, indicating continued efforts to combat some of the globe's most prevalent and chronic conditions, including cancers, HIV, Parkinson's and Alzheimer's disease, stroke and multiple sclerosis and influenza. New, reliable methods of population control and aids for ending nicotine dependency also featured. Bodies from the **US National Institutes of Health** (US NIH) were involved in five of these deals.

Notably, four transactions could have potential benefits for sufferers of Parkinson's disease and other severe neurological diseases. Amongst these was a licensing agreement made in August between **NuPathe** and the **University of Pennsylvania** for the LAD™ long-acting delivery technology (PDA no. 25046). This technology comprises a small, biodegradable polymer matrix, no larger than a grain of rice, which is positioned below the skin, from where it slowly releases its drug (over a 1-3 month period) before itself degrading. The controlled and sustained release would improve the efficacy of the treatment of Parkinson's disease and schizophrenia and reduce the risk of relapse in patients. The **Michael J. Fox Foundation for Parkinson's Research** granted **NeuroDerm** a fund of US\$0.49 M in May to support clinical work to develop a new transdermal skin patch for continuous delivery of Levodopa, the natural precursor of dopamine, which is deficient in Parkinson's disease (PDA no. 24222). It is hoped that the patch, through continuous transdermal delivery, will overcome the short half-life of Levodopa and should be able to minimise, or even reverse,

dyskinesias and other disabling late motor complications associated with long-term oral levodopa administration in advanced Parkinson's disease.

The Bioterrorism Threat

The threat of bioterrorism, against civilian populations and armies in the field, has impacted on the US Government's involvement in the pharmaceutical industry. During the last six months, the **US Department of Defense** has entered into two deals with the aim of combating this threat. In July, it awarded **LigoCyte Pharmaceuticals** a contract worth US\$2.3 M to continue its validation of its third-generation mucosal anthrax vaccine (PDA no. 24682). LigoCyte's dual-antigen vaccine includes a protein antigen to protect against a toxin released from the bacteria, and a bacterial capsule antigen to help the body fight the infection itself. This vaccine has a number of advantages over other anthrax vaccines currently being evaluated by the US government: the dry powder formulations are stable, easy to handle; it does not require cold storage and so can be transported to remote areas; the intranasal, needle-free delivery route is less invasive and could be self-administered; only a single dose would be required, in contrast to the six-dose regimen currently available. In October, the US Department of Defense awarded **Inovio Biomedical** a grant of US\$1.1 M to develop applications of its electroporation-based gene delivery technology for vaccination against infectious disease, including potential bioterrorism agents (PDA no. 25586).

Nanotechnology

Nanotechnology continues to account for a significant number of drug delivery deals; 9% of deals over this six-month period focused upon products which have, in some cases, been given a new lease of life due to the possibilities offered by delivery using nanotechnology. In particular, recent deals highlight the significance of nanotechnology's contribution to producing new formulations that enable the delivery of drugs transdermally, or the delivery of drugs that would otherwise be insoluble.

Global company Abbott Laboratories, in a partnership with **AstraZeneca**, was granted US rights in July to use **Elan's** proprietary NanoCrystal® technology (PDA no. 24681). This robust drug optimisation technology, which enables solubility, can be incorporated into common dosage forms, including tablets, capsules and inhalation devices. This agreement would use Elan's NanoCrystal® technology to develop and commercialise a single fixed-dose combination product containing the APIs in Abbott's TriCor® 145 (fenfibrate) and AstraZeneca's Crestor® (rosuvastatin calcium) products. Nanoparticles can also be used in pulmonary drug delivery. In May, the **Australian Research Council** awarded Singapore-based **NanoMaterials Technology** (NMT) and the **University of Sydney** a grant worth US\$333,000 to explore the market potential of drug delivery by inhalation aerosols using nanoparticles (PDA no. 24173).

Bridgehead Holdings International acquired the Asian rights in May to two reformulated cancer therapeutics which significantly reduce the toxicity and side-effects associated with the current versions of docetaxel and paclitaxel which use detergents to breakdown their compounds (PDA no. 24113). In addition to serious side-effects, this bleach also requires the immune system to be suppressed for three days, posing serious risks for cancer patients. The new formulation effectively removes the toxicity while, at the same time, enabling significant dosage increases.

Methods of Delivery

Methods of delivery varied considerably and included patches, sprays, inhalable products, liquids, gels, tablets, as well as more unusual technologies.

Five deals focused upon patches, including the NeuroDerm patch for Parkinson's disease discussed above. These included a joint development agreement made in May between **Nitto Denko** and **Eisai** concerning a transdermal adhesive preparation of Aricept® (donepezil hydrochloride), a drug currently indicated for mild-to-moderate Alzheimer's disease in tablet form (PDA no. 24221). This project aims to develop a transdermal patch formulation using Nitto Denko's proprietary transdermal delivery technology. The value of patches for pain relief is shown by **Lavipharm Laboratories'** fentanyl transdermal system, which can manage moderate to severe pain. In August, **DAVA Pharmaceuticals** agreed to be the exclusive marketer and distributor of the system in the US (PDA no. 25135).

Sprays, which deliver drugs safely and rapidly by nose or by mouth, have increasingly been developed by companies seeking user-friendly and effective alternatives to more invasive and unpleasant treatments. Five deals involved such sprays and all but one of these sprays was developed with the diabetes patient in mind. The potential improvement in the patient's quality of life is clear.

In August, **ShinNippon Biomedical Laboratories'** two subsidiaries, **Translational Research** and **Bioactis**, signed an agreement for the licensing and supplying their patented nasal drug delivery technology in the field of endocrinology to **Tokai Pharmaceuticals** (PDA no. 24955). This technology, an injection delivered through the nasal membrane, could be used for insulin or morphine. Between June and October, **Cardinal Health** participated in three deals involving sprays containing insulin products. The first, in June, saw Cardinal Health agree to formulate and fill clinical trial batches of **Generex Biotechnology's** Oral-lyn™, a proprietary oral insulin spray product (PDA no. 24594). Furthermore, in September, Cardinal Health agreed to distribute Generex Biotechnology's new Glucose RapidSpray™ product in the US (PDA no. 25295). This product delivers a fat-free, low-calorie glucose formulation directly into the mouth where it is rapidly absorbed into the bloodstream. It is intended to act as a companion product to Generex Oral-lyn™. The third deal, also in September,

gave **Bentley Pharmaceuticals** capacity at Cardinal Health's new North Raleigh facility, thereby enabling the scale-up and manufacture of clinical supplies of Bentley's intranasal product candidate which delivers insulin directly and discreetly through nasal mucosa (PDA no. 25305).

Six deals focused on inhalable products. These included **MAP Pharmaceuticals'** Tempo™ inhaler, a device which automatically adjusts to each patient's unique inspiration pattern, without electronics, and is very easy to use. In May, **Xemplar Pharmaceuticals** agreed to serve as the exclusive manufacturer of Tempo™ inhaler products currently being developed for the treatment of asthma and chronic obstructive pulmonary disease (COPD) (PDA no. 24274).

In July, **Antares Pahrham** signed a co-development agreement with the **Population Council** to develop contraceptive formulation products containing Nestorone® by using Antares' proprietary, advanced transdermal (ATD™) gel platform (PDA no. 24814). There are a number of advantages to this form of contraception: it is clear and cosmetically acceptable; it is safer than most oral contraceptives; it is convenient; it is attractive to women who have trouble taking oral contraceptives; it can be used when breastfeeding.

More unusual methods of drug delivery included the development of a chewing gum for the treatment of type 2 diabetes mellitus and obesity. Generex Biotechnology's buccal drug delivery platform technologies will be combined with **Fertin Pharma's** expertise in gum base formulations to develop a chewing gum that will deliver metformin into the body via the inner lining of the mouth (PDA no. 24396). This would avoid many of the unpleasant side-effects associated with taking this drug in tablet form and will offer a far more attractive option to young diabetics. Other products include the BEMA™ disc, which delivers pain relief to cancer patients directly through the inner cheek (BioDelivery Sciences International acquired all non-US rights to the product from QLT USA in August) (PDA no. 24931), and two toothpastes. **PharmaSpritz Corporation** and **AZ Technologies** will develop the F.A.S.T. toothpaste for weight loss and Pearly Dreams for sleep inducing (PDA no. 25121).

Conclusion

A broad range of delivery devices and technologies have formed the focus of drug delivery transactions during the last six months, ranging from inhalers and injectors, transdermal patches, creams and gels to liquids and tablets, foam and film, chewing gum and toothpaste. While the aim remains of adapting old products to new methods of delivery in order to expand their market life, it is also clear that producing a product that is easy to use, self-administering if possible, painless and convenient is a significant factor.

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