Is the pharmaceutical industry open for innovation?

Open innovation is the hot topic in many industries and this approach has the potential to make a radical difference to the costs of drug discovery and development in the pharmaceutical industry. But there are also barriers to the industry fully embracing this new way of working and adding it to other models for externalisation. This paper describes how open innovation is different from these other models and examines some of the exploratory models adopted by companies in this area. It is very early days but there are some signs that large pharmaceutical companies are willing to move to a more flexible, open way of working. Perhaps the greatest barriers to fully implementing open innovation in the pharmaceutical industry are cultural and there will need to be strong senior internal leadership in companies to ensure the required changes in mindset and behaviour are incentivised.

By Dr Jackie Hunter CBE

Almost every article on the pharmaceutical industry in the past five years has begun with a description of the pharmaceutical industry's slowness to develop new drugs and lack of productivity[1]. Despite the recent realisation that the productivity decline in the past decade is more a function of a peak in 1995-2000 (FDA data 1970-2008) than a true decline, the reality is that costs have escalated, and hence investment in R&D, with no concomitant increase in return on that investment[2,3]. It is also true that the biotechnology firms, upon which the large pharmaceutical companies rely for externally accessing new compounds, are also giving a relatively poor return on investment as a sector, despite the recent large sums paid by big companies for relatively early assets.

Initially pharmaceutical companies followed companies in other sectors and tried to solve the productivity gap by mergers and acquisitions. Through this companies hoped to find economies of scale and to improve their efficiency and productivity. Thus 29 of the companies that existed in 1980 now have reduced to nine global pharmaceutical giants. However, this strategy did not lead to the expected increases in new product approvals, nor did they lead to a reduction in costs per approval[1]. The pharmaceutical industry's current success rates are still not sufficient to sustain large internal R&D organisations, making the industry's current operating model financially non-viable[2]. Therefore companies are seeking new avenues to either increase their level of innovation, cut costs or reduce risk.

One strategy many major corporates have publically espoused is one of increasingly externalising their R&D through collaboration[3]. Traditionally this has been through large collaborations either with biotechnology companies,

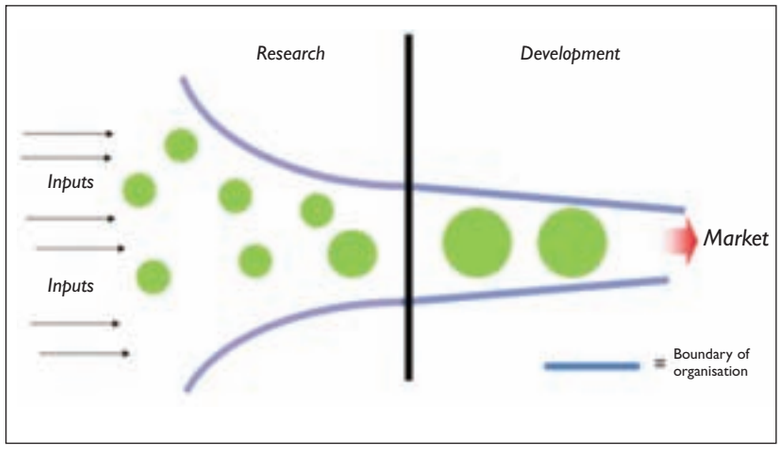

Figure 1a: Closed innovation model

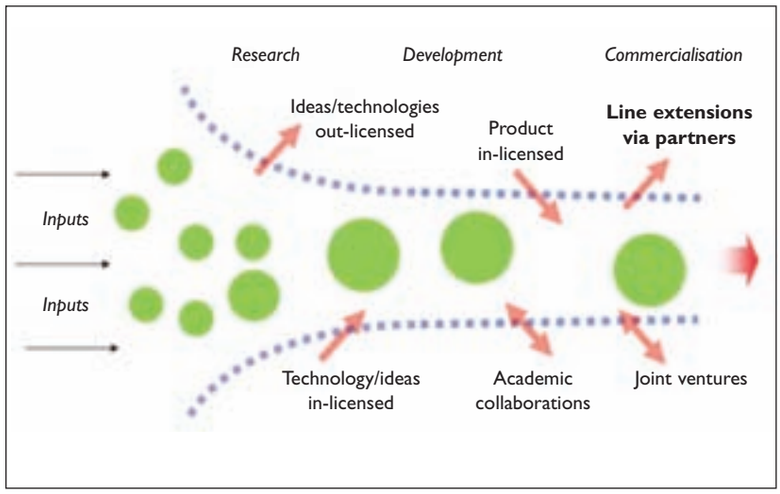

Figure 1b: Open innovation model

established academic institutions or via public private partnerships[4]. In the past few years there has been a large increase in public-private partnerships such as the Innovative Medicines Initiative[5] and the Biomarkers Consortium as well as other precompetitive collaborative initiatives led by industry, eg the Pistoia Alliance[6,7]. One emerging concept underpinning such collaborations is that of open innovation. Yet there seems to be a lot of confusion about what this actually means, especially when discussed in terms of the pharmaceutical industry.

The term open innovation was first coined by Henry Chesborough in 2003[8]. In it he defined open innovation as: *'The use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation, respectively. Open innovation is a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal, and external, paths to market, as they look to advance their technology'*. Joel West[9] sees it simply as: *'Open innovation means treating innovation like anything else – something that can be bought and sold on the open market, not just produced and used within the boundaries of the firm'*. At first reading this seems like a statement of the obvious – why would companies, especially pharmaceutical companies, not embrace such a concept as one of their key externalisation strategies?

Historically, the pharmaceutical industry has operated a traditional, closed model (**Figure 1a**) where a single company has all the means of prosecuting an idea from inception to market and all IP is retained within the company boundaries. In an open innovation model (**Figure 1b**), there is a much more dynamic ecosystem, with the boundaries of the organisation becoming much more porous. It is important to note the two-way nature of the interaction in the open innovation model. Many companies in the past, in both the pharmaceutical and other sectors, have concentrated on a uni-directional approach, sourcing from the outside in, instead of a bi-directional approach, where the outflows from an organisation are as an important source of innovation as the inflows. In terms of large pharmaceutical firms this can be clearly seen by the lack of spin-out companies across the sector. There have been some notable exceptions – for example the Swiss biotech sector was significantly stimulated by pharmaceutical spin-outs in the 1990s[10].

Barriers to open innovation

Many of the barriers to open innovation are also true to some extent for other forms of collaboration. These include issues of intellectual property protection (IP), lack of leadership and incentives and insufficient investment in collaborative infrastructure. One of the main barriers to the adoption of open innovation strategies by the pharmaceutical industry is lack of clarity about the implications for a company's intellectual property (IP). This is partly due to confusion between the terms 'open source' and 'open innovation'[11] and open source is often quoted as a model of open innovation[12]. However the fundamental difference between the two is that within a true open innovation paradigm, IP is not freely distributed but proactively managed and shared to create value that otherwise would not be realised to the participants of the open innovation collaborative network. In open source, IP is made freely available and thus benefits

can accrue to both collaborators and the wider community. There is clearly a place for open source collaborations in pharmaceutical R&D[13,14] and some new initiatives, such as the Open Pharmacological Space project proposed under the Innnovative Medicines Initiative, are exploring how this might work in early drug discovery[15]. In an open innovation model, the costs and benefits of innovation can be shared as well as the IP in line with the relative contribution of the various parties. This includes royalties and commercialisation rights but the IP rights are protected[16].

The pharmaceutical industry has rightly closely-guarded its IP but it is beginning to appreciate that there is a difference between hoarding or banking internal IP and managing it proactively to increase its use and productivity. For example, when company X ceases to work on a particular target Y, it would traditionally keep all the reagents, compounds and know-how around the target internal to the company. Longer term it would let the patents lapse and the reagents decay. In an open innovation paradigm, the company would either encourage internal employees to secure venture funding to spin the programme out, partner with academics or biotechnology companies to find new uses for the molecules or prosecute them in other ways, eg seeking non-traditional partners to commercialise the assets such as non-profit organisations. These approaches have worked well for companies in other sectors such as telecoms (British Telecom) and electronics (Philips).

There does need to be the appropriate environment for spin-outs and other vehicles to enable a true open innovation ecosystem to exist. The present global financial climate, especially that in Europe, has made the venture capital environment for pharmaceuticals much tougher than for other related industries, such as medical devices and consumer products, where the risks are less and the timelines to market much shorter. Companies such as Unilever and Philips have thriving venture capital arms that fund internal spin-outs as well as external companies and this has created a very vibrant open innovation ecosystem for these companies to access. Although many pharmaceutical companies have venture arms, few are concerned with spinning assets out or are looking to support projects very closely aligned with internal needs. Exceptions to this include Johnson and Johnson (J&J) and Merck.

Some other barriers exist outside of the confines of the pharmaceutical industry. For example, the willingness of other parties to adopt more flexible approaches to collaboration, funding and IP management is frequently seen as a barrier to adopting new ways of working including open innovation. Within biomedical academia there can still be wildly discrepant views on the value of commercialising their activities and collaboration with industry. Interestingly some of the challenges for industry are similar to those now faced by governments and other funding bodies in the light of the economic recession, ie how to get more innovation with less investment. In Dr Vince Cables' (Business Secretary, UK Coalition Government) recent speech on science funding at Queen Mary College (UK) (September 8, 2010), he highlighted the need for the UK to transform more research into innovation and for researchers to build stronger links between academia and industry. Historically many, but not all, of these interactions have been characterised by industry giving money to academics or academic centres without necessarily being very involved in the collaboration subsequently or expecting a return[4]. Now financial constraints mean that many companies are investing in such collaborations in a much more strategic way and are looking to obtain measurable returns on their investments.

The cultural change required to facilitate this new way of working should not be underestimated. Indeed many pharmaceutical companies need to increase their culture of collaboration and innovation internally before looking externally. The size of many companies precludes rapid data sharing[17] and paradoxically as companies organise themselves internally into smaller, competing units, this sharing can become even harder. It is important that managers are held accountable for finding the best solutions, wherever they occur. Proctor and Gamble's CEO AG Laffley would question employees who brought internally focused solutions to ensure that they had also considered all the potential external options. Some companies such as J&J have made it the remit of specific groups to ensure that not only are ideas from the outside routed to the appropriate group inside the company, but also that internal ideas are ferried across the company – in J&J's case this is the role of the Corporate Office of Science and Technology. Indeed, the success of external connectivity frequently depends on the presence of strong internal connections. Therefore it is vital that internal networks are well developed before an organisation embarks on a true open innovation strategy.

Finally it is vital that employees and managers at all levels are aware of the open innovation strategy, where it fits into the overall externalisation strategy for the organisation and are held accountable for

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implementing the strategy. Unfortunately timescales for realising value through these activities are longer in the pharmaceutical industry than in consumer goods or telecommunications. This sometimes makes it hard for employees who are also being asked to focus on timelines and portfolios to make the necessary time to also focus on accessing external knowledge or spinning ideas out of the company. Indeed in some cases these activities are still discouraged.

Existing examples of open innovation in the pharmaceutical industry

Patents and compounds

GlaxoSmithKline (GSK) has explored a number of different ways of interacting with both biotechnology companies and academia. In 2004, the Centre of Excellence for External Drug Discovery was established to form innovative deals with partners where risk and reward were shared, and also to make GSK capabilities or capacity available externally. Indeed a separate group called Scinovo was established to help partners source preclinical development studies. Innovative academic collaborations such as the initiatives with Imperial College (UK), Duke University (USA) and University of Pennsylvania (USA) allowed greater access to preclinical and clinical GSK compounds by investigators. In the case of the Imperial collaboration, substantial benefits could accrue to the academic and the university if their discoveries resulted in a new product or new use for a product. This concept has been refined with the establishment of the academic discovery performance unit which seeks to work with academics to explore novel uses for molecules that failed to achieve proof of concept in their chosen indication. A different approach, announced by GSK CEO Andrew Witty in 2009, consists of a patent pool for open innovation against neglected tropical diseases based at Tres Cantos in Spain. This was followed up by the release of >13,500 *in vitro* screening hits against malaria using Plasmodium falciparum along with their associated cytotoxicity data from an initial screen of more than two million compounds[18] and related data on >300,000 chemicals from an academic group was published in the same edition of the journal[19]. At the same time, Novartis also placed its Malaria Box data set of more than 5,600 compounds tested against the malaria parasite in the public domain[20]. This represents an important first step in making data sets more widely available. In terms of the patent pool for neglected diseases, contributors to the pool, including GSK, still retain the IP for other diseases and for countries outside the least developed countries. The further details and operating principles can be found in the pool's website (www.ntdpool.org).

Pfizer has allowed companies to screen against its internal library and Astra Zeneca recently signed a deal with the MRC-T to screen compounds from AZ's compound collection and compounds from the MRC-T (Medical Research Council-Technology, UK) on targets submitted by both parties. Although compound structures will not be disclosed, it is another step forward in sharing resources to 'co-create' additional value.

Crowd-sourcing initiatives

Lilly spun out InnoCentive in 2001 as the first global internet problem-solving platform designed to connect companies with challenging research problems 'seekers' with potential 'solvers' who would come up with solutions to these problems. There were several factors critical to the success of this initiative. InnoCentive was designed to have a very carefully defined governance structure to protect the IP of the seeker and the solver. It uses an interface and process that reduces the barriers to participation and allows for a rapid scale-up of activity. This, in turn, means it can reach out to a very diverse, global group of solvers. Since 2001, 170,000 people have participated, 800 problems have been posted and 400 problems have been solved. A recent study found a 29.5% success rate for problems where internal staff could find no solution[21]. InnoCentive has announced a partnership with the Nature publishing group to increase visibility and access and is also now being used internally in Lilly. Other companies have bespoke internal crowd-sourcing approaches such as Pfizer's Idea Farm.

GSK's consumer division has successfully implemented an open innovation strategy and 10 out of the current 11 top brands began as collaborations through their collaborative website. They seek innovative solutions to needs posted on their website. The learnings from such collaborations can lead to subsequent improvements in the collaborative process and a case history has been published[22].

Sharing of expertise

Lilly announced in June 2009 an initiative to make its assays and expertise available to academia to source new collaborations and compounds. This Phenotypic Drug Discovery Initiative (PD2) will make Lilly assays available to external collaborators to test their compounds. The stated goal of PD2 is to foster open collaboration between Lilly and global laboratory researchers in Alzheimer's

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disease, cancer, diabetes and osteoporosis. According to Lilly press releases and presentations, academic researchers submit their compound through an automated PD2 interface. The compound structure is evaluated by Lilly using a set of proprietary algorithms that focus on drug-like properties and structural novelty. If the compound structure meets certain criteria, the researcher is then invited to submit a physical sample for biological testing. In return for the biological data generated, Lilly has first rights to negotiate a collaboration or licensing agreement. If Lilly decides not to pursue the opportunity, then the researcher is granted ownership of the data report.

In 2009, GSK announced its intention to create an open innovation bioscience park at the GSK R&D facility in Stevenage, UK where companies located on the park will have access to specialist skills and technologies as well as mentoring from experienced drug discovery and development employees.

Other companies have stated their intention to move further in the direction of open innovation. Johnson and Johnson's Head of Pharma R&D Paul Stoffels stated in February 2009 "we are shifting our innovation ecosystem towards an open innovation model tapping into both institutes of scientific excellence and our own R&D centres across the world …taking a networked approach... increasingly with external public and private partners to generate ideas and intellectual property".

To conclude

Open innovation is a way of working that differs in that it is not open source or IP naïve but seeks to manage and use IP in a more productive way to innovate from early on in R&D through to commercialisation. It has provided tangible benefits in other sectors and could also do so for the pharmaceutical industry, although the timelines are much longer. Leadership within companies is critical – leaders at all levels need to communicate a clear open innovation strategy and define and resource the processes to implement the strategy. Excellence in partnering and collaborating are also important in the success of an open innovation strategy, with the appropriate metrics and recognition for those involved. DDW

Dr Jackie Hunter *has worked in the pharmaceutical industry for more than 25 years and in 2002 was appointed SVP and Head of the Neurology and Gastrointestinal Centre of Excellence (CEDD) for GlaxoSmithKline. The CEDD was focused on the development of new therapeutics for neurodegenerative disorders, pain and gastrointestinal diseases such as inflammatory bowel disease. In 2008 Dr Hunter became Head of Science Environment Development where she was responsible for developing an R&D strategy for precompetitive research and worked with external scientific partners. She established GSK as a leader in open innovation and led the creation of the world's first 'open innovation' campus for the pharmaceutical industry in Stevenage, UK. She also played a leading role in the establishment of the Innovative Medicines Initiative in Europe and chaired the EFPIA Research Directors Group. Dr Hunter left GSK in 2010 forming Pharmivation Ltd, to concentrate on open innovation in bioscience. She is also non-executive director of Proximagen Neuroscience. She was named as one of 2010's Women of Outstanding Achievement in Science, Engineering and Technology for her contribution to innovation and entrepreneurship and was awarded the CBE in June for her contributions to the pharmaceutical industry.*