Realizing open innovation

7.2

Paul Rodgers and Bill Primrose at Ithaka review the opportunities and challenges in opening up the innovation process in the pharmaceutical industry

Adoption of open innovation models by the pharmaceutical industry and the biomedical research community is a response to growing challenges in bringing new therapies into clinical use and securing an adequate return on investment. Open innovation in drug discovery and development is a term encompassing elements otherwise previously incorporated into licensing, collaboration and research grant funding as the industry seeks to assimilate ideas, intellectual property (IP) and innovation from a wider constituency than previously. Sources of innovation can include internal R&D, other companies (both large and small), academics and clinicians, funded from a range of sources, including the public purse, charities and industry.

These new approaches are rich in potential and are producing a steady stream of innovations that offer the promise of revolutionary developments. However, practitioners of open innovation face a number of significant challenges in bringing the resulting products and services to market. These challenges can be overcome but it requires resilience, adaptability and creativity to do so. Ownership of existing and developed IP is a key issue. Questions arise as to who brings what to the consortium, who benefits from newly created IP and who has the rights to exploit it. This chapter gives a background to the questions inherent within open innovation in the pharmaceutical industry, and provides a number of examples of how it is being addressed.

Why the pharmaceutical industry embraces open innovation

The pharmaceutical industry (Pharma) has undergone a sea change in recent years with regard to its willingness to embrace open innovation. Whereas a decade ago the R&D culture was one of maintaining confidentiality come what may, the industry is now exploring a wide range of open innovation models. This has largely been driven by a 10-fold increase in the cost of developing new drugs over the past three decades, with R&D productivity at a historic low over the same period.

Pharma is good at many things. It has access to finance, plus a reservoir of tools and resources (including large, diverse screening libraries and clinical databases) and technical expertise that are not available to early-stage companies. It has staff with significant knowledge of the whole drug discovery and development process, whose experience is a valuable asset if shared with others. It has the money and global reach to carry out all phases of clinical trials, and to market and sell the resultant drugs. However, it is increasingly lacking in the innovation necessary to discover new drug candidates.

Pharma can be considered now as being similar to large manufacturing companies, funded through sales and equity markets, but requiring that the new clinical candidates to feed its pipeline be sourced from elsewhere. Traditional licensing deals with smaller biotechnology companies remain important, but Pharma is also now interacting directly with academics, other global pharmaceutical companies, charities and publicly funded health initiatives to source innovation, predominantly in the pre-clinical area. New approaches are being used to identify novel targets and optimize processes, and input is required from this larger number of players. These new approaches are rich in potential and are producing a steady stream of innovations that offer the promise of revolutionary developments.

Models for open innovation

For drug discovery and development, we can consider two different models of open innovation dependent on the type of clinical indication being addressed:

1. those indications with a large market where a sufficient product price is achievable for Pharma to want to develop, market and sell their own products ('mainstream indications'); and
2. indications where the market is small, or where reimbursement is low, but where the pressure for new treatments is driven by public health or societal reasons ('neglected indications'). These latter indications include some infectious diseases in the developed world and many diseases that are prevalent in the developing world. It may be that successes in this category will encourage Pharma to become more involved in open innovation activities for mainstream indications in due course.

Table 7.2.1 summarizes some examples of open innovation initiatives for neglected indications and Table 7.2.2 provides examples of open innovation in the field of mainstream indications.

TABLE 7.2.1 Examples of open innovation in neglected indications

Example	Participants	Notes
Tres Cantos Open Lab Foundation: Malaria Drug Discovery (**www.openlabfoundation.org**)	GlaxoSmithKline (GSK), Novartis, St Jude Children's Research Hospital and others	A combined library of more than 20,000 compounds with some anti-malarial activity was made available for researchers to identify starting points for further lead optimization
NewDrugs4BadBugs: antibiotics discovery and development	Innovative Medicines Initiative (IMI), AstraZeneca (AZ), GSK, Janssen, Sanofi and Basilea Pharmaceutica, and others	Project budget of €223.7 million. Data and knowledge sharing to learn from previous antibiotic development efforts, particularly from failures, which are not normally made public
Tuberculosis (TB) Drug Accelerator (**www.astrazeneca.com/Research/news/Article/25062012–seven-pharmaceutical-companies-join-academic-research**)	Abbott, AZ, Bayer, Eli Lilly, GSK, Merck, Sanofi, Infectious Disease Research Institute; National Institute of Allergy & Infectious Diseases, Texas A&M University; and Weill Cornell Medical College	$20m funding from the Bill & Melinda Gates Foundation; Pharma will open up selected sections of their compound libraries and share data with each other and the four research institutions; the companies will work together to develop the best prospects, regardless of where the drug originated
WIPO Re:Search (**www.wipo.int/research/en/**)	Collaboration of private and public sector organizations sponsored by the World Intellectual Property Organization (WIPO) in collaboration with BIO Ventures for Global Health	Development of new and better treatments against neglected tropical diseases such as dengue, rabies and Chagas disease, as well as malaria and TB

TABLE 7.2.2 Examples of open innovation in mainstream indications

Example	Participants	Notes
Critical Path Institute (C-Path, **www.c-path.org/consortia.cfm**)	C-Path partnerships include more than 1,000 scientists from government regulatory agencies (eg FDA), academia, patient advocacy organizations, and 41 major pharmaceutical companies	C-Path improves efficiency of the development of drugs, diagnostics and medical devices by creating new data standards, measurement standards and methods standards
European Lead Factory (**www.imi.europa.eu/content/european-lead-factory**)	IMI, 30 academic and industry partners, including Bayer, Janssen, Merck-Serono, AZ, Sanofi, UCB and Lundbeck	€196 million initiative combines a 500,000-compound library and a high-throughput screening (HTS) centre against novel targets proposed by academic groups
Compound library sharing (reported in: *Nature Rev. Drug Disc.*, 2012, 11, 239)	AZ and Bayer	Agreed to make their entire compound libraries (4 million molecules) available to one another for HTS runs
Drug repurposing (**www.mrc.ac.uk/Newspublications/News/MRC008918**)	UK Medical Research Council (MRC) and AZ	£10 million from MRC to provide UK academics with the means to study 22 compounds, de-prioritized by AZ, for new indications
TransCelerate Biopharma (**www.transceleratebiopharmainc.com**)	Abbott, AZ, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, GSK, Johnson & Johnson, Pfizer, Genentech and Sanofi	A non-profit organization set up for precompetitive research to address long-standing challenges in new drug development
Stevenage Bioscience Catalyst (SBC, **www.stevenagecatalyst.com**)	Cambridge University and GSK	University researchers will be based at SBC, the UK's first open innovation bioscience campus, co-located with GSK's R&D centre to advance drug discovery and development of new medicines

An open innovation consortium may have R&D contributions from a number of different members, broadly described as ACEs (academic centres of excellence), SMEs (looking to apply internal and acquired innovation to support the needs of larger companies, and with a mix of public and private funding sources), and the Pharma industry.

It is important to distinguish between open innovation and open access. Fundamentally, open access is a one-way, giving process whereby data and information are made freely available to all comers in the hope that this will stimulate innovation. For example, GSK announced in December 2012 its intention to release 'patient-level' raw data from clinical trials of approved drugs and failed investigational compounds. This move, which will begin in 2013, could catalyse a growth in the understanding of disease and help avoid repeating mistakes made in failed trials, particularly if other companies follow GSK's lead.

What are the current commercial and technical limitations on realizing the potential of open innovation?

Potential commercial limitations include the following:

1. *Funding*. Finance is required to bring any innovation to market, but in drug discovery and development, the required investment can be daunting – hundreds of millions of dollars, perhaps up to $2 billion for a new drug, can be spent commercializing an innovation. Timescales are also daunting: it can take 12–14 years to bring a new therapeutic to market. Even a full hit-to-lead optimization project can take up to two years and cost $2.5 million. Attrition rates are enormous: only one out of every 10,000 novel compounds originally screened for a beneficial therapeutic effect eventually makes it to market, and as many as 30 projects need to be initiated to bring one to fruition. The long timescales and high levels of risk combine to make securing adequate funding a particularly onerous challenge.
2. *Benefits*. While the overall goal of delivering new treatments and 'making a difference' is common to all the participants involved in an open innovation consortium, the rewards for each are different and they may lead to tensions within the partnership as each participant seeks to realize its desired rewards. The benefits for each member of an open innovation consortium may be:
   - academic institutions – increasingly look for a commercial return on their research, which has been funded through the public purse;
   - academics – funding, scientific interest, publications, career advancement;
   - clinicians – new treatments, funding;
   - governments – societal benefits, control of healthcare budget;
   - non-profit organizations such as medical research foundations and charities – new treatments for specific disease(s);

- SMEs – funding, service provision, opportunities for licensing and trade sale;
- Pharma – new compounds to fill pipeline, sales, licensing opportunities and, in the case of neglected indications, positive publicity for working on diseases of the developing world.

3 *Business model.* As discussed, the risks and timescales make it virtually impossible for a start-up company to take an innovation all the way to market on its own. Typically, the innovator requires to seek a partner with deep pockets to commercialize the product and provide the innovator with an earlier (though smaller) financial return. However, this brings new challenges with regard to issues such as loss of control, poor communication, different expectations and culture clashes that can cause partnerships to fall apart.

4 *Intellectual property.* IP contributions to the consortium may come from a number of sources, including Pharma, SMEs, research foundations and academia. This background IP may need to be made available to the other participants during the course of the project and appropriate licensing will need to be put in place. IP created during the course of the project (foreground IP) may require access to the appropriate background IP in order for it to be exploitable, and this will also need to be addressed in any initial consortium agreement. The right to exploit the outputs of the consortium will also need to be addressed. In general, this will be carried out by an industry player, and Pharma is likely to have the expertise to do this most straightforwardly.

5 *Management*. There are multiple challenges in managing a consortium of partners with different visions, goals and motivation. These challenges can be magnified by cultural differences between industry, academia, charities and healthcare providers, and further exacerbated by cultural and language issues in international partnerships. Highly skilled and experienced project managers are required, but they can be thin on the ground.

Technical issues include the following:

1 *Sharing of data, know-how, materials and equipment.* For a partnership to be successful, proprietary data, know-how and materials will likely need to be exchanged or shared. The owning party will require comfort that there are mechanisms in place to ensure that there is no 'leakage' to organizations outside the consortium. All parties will want clarity on who owns any improvements and derivatives, and equitable arrangements for sharing of resultant benefits.

2 *Fit for purpose*. Procedures need to be implemented for making project management decisions on issues such as whether a jointly developed product or service is fit for purpose.

3 *Clear pathway to regulatory approval.* There are challenges in meeting regulatory standards with products arising from consortia or from open source developments. How are standardization and traceability of data and reporting, records etc achieved across a partnership when some of the partners may have little or no previous relevant experience of regulatory issues?

The limitations and challenges outlined above require new approaches and this is driving the development and implementation of new innovation models.

Conclusions

Drug discovery and development is a sector with a need for collaborative approaches to innovation yet it faces so many perceived barriers – worries around IP, business models, competitive funding schemes and so on. It is clear that successful open innovation requires careful planning in order to align the partners' goals and expectations, and to develop procedures and guidelines to address the barriers mentioned above. However, the ultimate key to success lies in the participants understanding each other in order to succeed together. This requires the development of mutual trust, which can only be fostered through understanding your collaborator(s), which in turn can only be built through engagement with that collaborator(s).

CASE STUDY

Psynova Neurotech Ltd (**www.psynova.com**) was founded in 2005 by Dr Sabine Bahn and Prof Chris Lowe of Cambridge University with support from Paul Rodgers who then served as Chairman of the Board until its acquisition by Myriad Genetics in 2011. The company is developing novel protein biomarkers for neuropsychiatric disorders and is a participant in the IMI NEWMEDS (Novel Methods leading to New Medications in Depression and Schizophrenia) programme. NEWMEDS (**www.newmeds-europe.com**) is an international consortium of scientists which has launched one of the largest research academic-industry collaboration projects to find new methods for the development of drugs for schizophrenia and depression. Participants include Pharma companies, academia and SMEs.

The participating companies pooled their data into a large collaborative dataset that brings together the data of 23,401 anonymized patients from 67 trials on 11 compounds in over 25 countries. This makes it by far the largest single database of clinical trial data ever amassed in psychiatric research. Access to this database, plus access to clinical samples, was of major benefit to Psynova for validating its novel biomarkers. The consortium facilitated development of relationships with Pharma companies, which resulted in a very real and tangible benefit for Psynova in the form of a significant licensing deal with Roche on a schizophrenia biomarker.

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