

Breathing new life into pharma's innovation engine

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It has become common wisdom that pharmaceutical companies can no longer rely on their internal R&D departments to maintain the flow of innovative medicines through the pipeline.

Academic researchers clearly bring a deep understanding of disease biology across the whole range of human ailments that is impossible to replicate with the same breadth internally, and for many years pharma companies have forged collaborations to tap into their expertise.

In recent years there has however been a shift away from ad hoc licensing arrangements between pharma and academia towards higher-level strategic collaborations.

Barbara Slusher, director of the Academic Drug Discovery Consortium (ADDC) - an initiative set up in 2012 to coordinate the activities of scientists and centres around the world - believes one factor behind this is the dramatic increase in the amount of drug discovery work being done in academia over the last decade.

“There used to be a handful of academic drug discovery centres, but today there are almost 100 in the US alone,” she said, adding that in some high-risk fields such as neuroscience this is happening because the pharma industry as a whole is reducing its investment.

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Given that many university research departments are under similar cost pressures to industry as grant funding becomes ever tighter, there is a pull on both sides to work more closely and share risk on early translational work.

Slusher's primary job is director of the NeuroTranslational Drug Discovery Program at the Brain Science Institute (BSI) at Johns Hopkins University in the US, which has had a wide-ranging collaboration with Japanese pharma company Eisai since 2011 that exemplifies the changing nature of pharma-academic

projects. The BSI brings novel targets and assays to Eisai, which screens its compound library against them. Then, in something of a departure from the conventional model - Eisai then gives compound hits back to the BSI.

“We're taking over a lot of the drug discovery effort, and Eisai only gets involved if that is successful,” said Slusher, adding this leads to more risk-sharing but also a higher level of co-ownership of intellectual property (IP).

Another approach is to get researchers to come to you via the creation of competitions or challenges, with the lure of cash prizes or lucrative collaborations.

One of the proponents of this approach is GlaxoSmithKline (GSK), which has established a department known as DPAC - Discovery Partnerships with Academia - to help track down promising science within academia and to provide a structure whereby academic partners could become core members of drug discovery teams.

DPAC runs an innovation challenge called the Discovery Fast Track to help broaden the reach of DPAC. Researchers are invited to submit projects - with preliminary supporting assay data - to a panel of GSK reviewers. Those shortlisted get the opportunity to present their hypothesis to the company and - for a lucky few - collaboration with the DPAC team, including access to GSK's compound collection to screen for molecules and input from GSK scientists to help identify suitable drug candidates.

“Discovery Fast Track provides the focus and process for us to reach a large number of academic researchers that we would not be able to do if we were visiting each individual university or institute,” said Duncan Holmes, European head of DPAC.

The competition has not been entirely without critics, with early concerns that the terms and conditions (T&Cs) of participation may conflict with their IP policies. The University of California Los Angeles (UCLA) asked its scientists not to participate initially, although it seems now its fears about IP have been reconciled via some tinkering with the T&C wording.

The challenge has helped GSK establish a simple process for agreeing collaborations so that there is no need for protracted negotiations, and the initial submission is a one-page, non-confidential proposal with the involvement of the institution's technical transfer office, according to Holmes.

“All of this helps us to access the most promising early stage science, with minimum bureaucracy,” he said. To date, the Discovery Challenge and other DPAC activities have led to the inception of 10 projects in collaboration with academic researchers in the UK, France, Israel, the US and Canada.

Similar challenges have been set up by other pharmaceutical companies, albeit generally on a much smaller scale. To give just two examples, AZ sponsors the Innovate Competition to students working in the area of basic and translational research, while Merck & Co runs a challenge to statisticians who can come up with improved ways of predicting the biological activities of molecules.

Two-way street

Regardless of the potential rewards, academic scientists do need to be mindful of the pitfalls of getting involved with a commercial partner too soon, according to Slusher. For instance, academics are typically rewarded on the basis of publishing research, so adapting to a programme where information has to be held back for IP purposes can be a challenge.

One way to reconcile the changes is to adopt a double track to compound discovery, identifying tool compounds that can be published and disseminated to aid drug discovery research alongside unshared, 'druggable' candidates.

Participation also requires commitment at an early stage in the gestation of a research project and there are concerns that for academic researchers - often with limited or zero industrial experience - valuable time, expertise and IP might be given away too cheaply. That is a receding issue however as

more and more industry researchers make the switch to academia - thanks in part to cuts in internal R&D budgets.

Moreover, as more and more companies go down an external R&D route, it can also be hard for researchers in top-tier projects to make a decision about which partner to sign up with, given that some universities may be hosting multiple pharma companies every month.

“Each company will have a different approach and culture, and therefore academics should explore which fits better with what they are looking for,” said Holmes.

Getting close to the action

Another collaborative model being adopted by some companies is to place their own staff in close proximity to 'hot spots' of academic excellence, encouraging dialogue between external and internal researchers.

Johnson & Johnson is one trying this approach, setting up a network of innovation hubs and satellite offices in California, Boston, London and Shanghai. Merck has taken a slightly different tack, setting up the independent, non-profit California Institute for Biomedical Research (Calibr) to offer academic scientists a path for translating their biomedical research into novel medicines. A version of the latter model is also being explored by Almac, which recently agreed to set up a joint drug discovery facility with Queen's University Belfast in Northern Ireland.

Meanwhile, AZ has taken yet another route to externalising R&D via its virtual iMED programme, which was set up in 2012 as a result of the company's decision to call a halt to internal research in the neuroscience field. This virtual operation means that AZ relies on a small team of talent scouts to identify early-stage drug discoveries and usher them through proof-of-concept. The result is that the company can take a broader view than a stand-alone R&D department, bringing forward any project that looks like it can bring a good return on investment, including smaller indications than it has considered in the past.

Open source

What is clear however is that - despite new approaches to academic collaboration - the long-term objective for pharma companies is still to bring promising projects behind the internal R&D firewall. As such the industry is still quite a long way away from implementing a true 'open innovation' approach to drug discovery.

“In academic collaborations such as DPAC, GSK makes all decisions together with research collaborators and openly shares data with them,” noted Holmes. “We run the projects just as if they were GSK internal projects but with the difference that our academic collaborators are an integral part of the team,” he added.

Some form of open innovation or pre-competitive collaboration is starting to emerge in projects such as the Innovative Medicines Initiative (IMI) founded by the European Commission and European Federation of Pharmaceutical Industries and Associations (EFPIA) - which is focusing on neglected areas such as antibiotics research - helped by drugs donated by pharma companies - and tackling bottlenecks in the R&D process.

There are also examples of companies opening up their compound libraries and disease-and target-relevant assays to external researchers and - more recently - preliminary moves towards sharing patient-level data from clinical trials, such as the Project Data Sphere consortium that is sharing phase III trial results in cancer.

Whether these new forms of collaboration ultimately lead to a paradigm shift in medicines research towards a more open model remains to be seen.

“The verdict is still out as to whether this will be a better way to do drug discovery,” according to

Slusher.