



Drug discovery: new models for industry–academic partnerships

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The re-focusing of pharmaceutical industry research away from early discovery activities is stimulating the development of novel models of drug discovery, notably involving academia as a ‘front end’. In this article the authors explore the drivers of change, the role of new entrants (universities with specialised core facilities) and novel partnership models. If they are to be sustainable and deliver, these new models must be flexible and properly funded by industry or public funding, rewarding all partners for contributions. The introduction of an industry-like process and experienced management teams signals a revolution in discovery that benefits society by improving the value gained from publicly funded research.

Introduction

The drug discovery industry is facing considerable challenges due to increasing costs, decreasing productivity and attrition of projects as they progress through the development process [1]. Companies are responding with extensive re-organisation, restructuring and re-focusing in order to address the issues around R&D productivity, process inefficiency, project attrition and the increasing costs of taking a potential new drug to the market and to secure profits when providing for smaller patient populations [2].

The changes are leading to a mixed model for drug discovery driven by great opportunities for new entrants into the drug discovery space. While biotechnology companies and small and medium entities (SMEs) have increasingly been involved in partnerships over the past 10 years [16], new entrants – including university-based drug discovery groups – offer potential solutions to the gaps in the drug discovery environment. Academic research has traditionally been the home of research innovation and universities are powerhouses of innovative drug target-based discovery and disease knowledge. It is accepted that industry has not succeeded in fully realising the potential of academic research in the past [1]. This failure stands to be replicated without novel and forward-thinking approaches towards linking academic and indus-

trial drug discovery research to exploit, fully and efficiently, the potential of both sectors to the benefit of all.

Changing models of discovery in the pharmaceutical industry

The productivity challenge in pharma is generally attributed to rising expenditure on R&D, against a background of falling output and depleted pipelines. The industry spends over \$30 billion every year on R&D, a thirty-fold increase since 1970 [2–5]. This fundamental decline in efficiency results from macroeconomic technological and scientific changes, along with structural changes arising from companies’ internal strategic and operational practices [6].

The pharma industry has to move from business plans mainly focused on finding and marketing the big blockbuster (greater than \$1 billion/year sales) towards one that will provide adequate profits from smaller ‘orphan’ patient populations (less than 200 000). This has been driven partly by the genomics revolution that predicted that knowing all of the molecular targets and proteins involved in diseases would lead to a host of novel therapies. So far this has failed to deliver as it has become clear that the mainstream market diseases are more complex than initially thought. The combinatorial chemistry and high-throughput approach to finding new chemical leads has also failed to deliver significantly to date [1]. Many targets that look good in early animal or *in vitro* studies have also failed to translate to the clinic.

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This is probably due to poor understanding of the disease processes being targeted. George Brewer, in his 2006 review, predicted that 'productivity (from the current approaches) will be on the order of half or less that needed to sustain the pharmaceutical industry as it is currently constituted' [2].

All of these issues have led to increasing pressure on the industry. Governments and commercial players are driving a global trend towards cost containment. The pressure comes from numerous directions, including, for example, pricing and reimbursement practices, mandation of generics and legislation to encourage parallel importation [7]. The devolution of power to commercial or regional stakeholders, such as primary care trusts in the UK, has rendered the healthcare market increasingly complex [8].

Additionally, pharmaceutical companies have had to cope with a slow and inefficient regulatory process, and shareholder expectations of high return, fostered by the development of a 'blockbuster culture' in which only products with peak sales in excess of \$1 billion a year are considered viable [9]. Their R&D organisations have had to cope with an explosion of scientific knowledge and technologies, but they have been hampered by a non-entrepreneurial culture—the result of 'merger mania', the need to reduce financial risk and enhance return, organisational divides between 'research' and 'development' and, in some cases, poor management [9].

These pressures have resulted in companies enhancing their focus on 'D' and withdrawing, to some degree, from 'R', leading to a decline in their ability to innovate in discovery activities. There has been a consequent reduction in the volume and novelty of their development and clinical pipelines [10].

The pharmaceutical industry is constantly driven by the need to maintain and increase successful product development levels and shareholder value. The growth of medium to large firms in the 1980s and 1990s was followed by a series of mergers to form the large cross-therapeutic area discovery and development multinationals of the past five to 10 years [16]. Giants, such as GlaxoSmithKline, AstraZeneca, Pfizer and Sanofi Aventis, are each offering large and broad therapeutic portfolios, yet they still strive for further growth in order to maintain the promised returns to their shareholders. The next stage of growth is now under way in an attempt to boost the number of new therapeutic entities discovered, developed, registered and marketed and thereby to maintain the profits of the past and tackle the challenges of tomorrow (<http://www.gsk.com/>, <http://www.astrazeneca.com/>, <http://www.pfizer.co.uk/>, <http://www.sanofi-aventis.com/>).

Small and medium-sized biotechnology and pharmaceutical enterprises with closer links between research and development have been more successful than their big sisters at moving candidates through the development pipeline. In particular, they have been better at producing biological products, such as monoclonal antibodies, vaccines and peptides, to tackle unmet needs in the market [11,12].

The giants are responding in a variety of ways: (a) focusing internal discovery efforts on lower-risk projects to improve therapies incrementally in large market indications; (b) increasing the efficiency of the development process and decreasing compound (and therefore project) attrition; (c) in-licensing technology platforms, validated targets and lead compounds or candidates from other (usually smaller) organisations; and (d) adopting new inter-

nal management structures to replicate the perceived success and efficiency of SMEs. We note that although large pharmaceutical companies are still committing huge budgets to R&D, on the whole they are decreasing their focus on the early stages of target discovery and validation and re-focusing on later-stage development, which is a major factor in driving the recent and continuing stream of R&D redundancies [12,13].

These actions in themselves, though, are unlikely to satisfy voracious pipeline requirements or to provide the truly novel and innovative approaches needed to treat large areas of unmet needs in hard to treat, resistant and diseases that affect the developing world [14,15]. These diseases are, on the whole, not commercially viable for industry and, thus, publicly funded research should be encouraged to work in these areas. New sources of innovation are required and many large companies are looking for inspiration externally.

Yet, while relationships between pharma and biotech are well known [15], the emerging R&D partnerships between pharmaceutical companies and academic institutions are less well documented. In particular, new models of interaction with research institutes and universities are emerging to help fill the gap in pharma pipelines and complement other activities to address major new areas of research with the potential for major new product lines. Although fragmented in its structure, this evolving drug discovery model is attractive because risks can be mitigated by sharing resources with partners.

New R&D partnerships to access new sources of innovation

Industry has always worked with third parties to access specific technology and expertise. Now, though, it also needs to access an expanded set of requirements: novel targets, target types and signalling pathways, disease expertise, human cells and tissues for target validation studies, patients for earlier and earlier clinical safety and efficacy studies, platform technologies, novel chemistries, disease and pharmacology biomarker development and biotechnology processing.

Traditional academic research funded by grant bodies and research councils continues to provide a pipeline of inventions and product ideas available for licensing, as demonstrated by the success of university technology transfer groups such as the Medical Research Council Technology (<http://www.mrctechnology.org/>), Cancer Research Technology (<http://www.cancertechnology.co.uk/>), IP Group (<http://www.ipgroupplc.com/>) and Imperial Innovations (<http://www.imperialinnovations.co.uk/>) [17,18,19]. Despite a long tradition of pharmaceutical collaborations, however, universities have not been credited as major players in this sector. Rather, companies have defined and financed research projects using university staff and resources and appropriated value from these projects by taking ownership of the arising intellectual property, and paying royalties on sales if products are commercially successful [20]. We have found that these types of R&D partnerships tend to be at arm's length and do not necessarily offer a reliable pipeline of innovation for pharmaceutical R&D. Academic scientists tend to be driven by academic research questions that need to be carefully aligned with the commercial interests of their colleagues in industry [21]. Cultural differences between university technology transfer groups and industry in-licensing teams in the past have led

to undue effort being expended on technologies of limited interest to industry, and government or other grant funding for research with commercial interest has been hard to come by. As a result, many novel targets will undoubtedly have fallen by the wayside and into a so-called translational gap.

This situation is now changing with a growing realisation that one interest very much at the heart of both academic and industrial scientists is the desire to provide better treatment and care to patients in the clinic and the surgery. With this in mind, industry and academia are now working together to develop new partnerships to bridge the translational gap and form a new 'front end' to the early discovery phase of drug development. Universities are showing themselves to be capable of delivering new therapeutic entities to focused and efficient companies that can take these through pre-clinical and clinical development. A notable success in this area is the development of anti-TNF α antibodies (etanercept, infliximab and adalimumab) for rheumatoid arthritis and psoriasis, based on target identification at the Kennedy Institute, Imperial College London [22]. Similarly, for some time Cancer Research UK/Cancer Research Technology has been funding and working with academic–industry partnerships to deliver over 100 novel agents into clinical evaluation, including Temozolamide, Carboplatin, Tomudex and Zinecard [23]. New compounds developed by new academic drug discovery groups are likely to come on stream in the clinic in future [23].

To make these partnerships work financially, and make the research count, the early work must be properly funded and the rewards shared equitably. Commercial investors, including pharmaceutical companies, are understandably reluctant to bear the full cost of this risky and sometimes long-term work for the reasons mentioned above, so government funding bodies and charitable institutions have recently begun to open their doors to these projects. Innovative funding programmes such as the Wellcome Trust's £91 million Seeding Drug Discovery initiative, the more recent Medical Research Council Developmental Pathway Funding Scheme and the EU Innovative Medicines Initiative, now cover both basic and translational research and offer our new entrants opportunities to access their new ideas in drug discovery (<http://www.wellcome.ac.uk/>, <http://www.mrc.ac.uk/>, <http://www.imi.europa.eu/>). Industry with a direct interest in the outcome is also expected to contribute [24,25]. Charities also put significant funding streams into drug discovery efforts, often focusing on specific disease areas such as malaria and TB for the Bill & Melinda Gates Foundation (<http://www.gatesfoundation.org/>) and Trypanosomiasis, Leishmaniasis and Chagas diseases for the Drugs for Neglected Diseases Initiative (<http://www.dndi.org/>). However, further funding is still required to effectively translate the wealth of basic research into reality.

We contend that pharma and academia need each other to bridge the translational gap. In partnership with each other and with the biotech industry they can form a new 'front end' to the early discovery phase of drug development, delivering new therapeutic entities to focused and efficient companies that can take these through pre-clinical and clinical development to the market.

We believe that a more systematic approach can ensure that these partnerships are sustainable in the longer term and provide greater encouragement for new entrants to participate, greatly

increasing the overall research output in this area. While industry will fund and manage the expensive clinical phases, their partners will encourage innovative research and the development of 'disruptive technologies' that will change the face of drug discovery.

Novel partnering models to increase innovation in pharmaceutical R&D

Partnering of pharma with external research organisations has grown gradually and organically as companies have begun to accept the limitations of their research activities. The range of partnering options is becoming broader and the recognition of external contributions is better recognised.

Companies have turned to the outsourcing of specific activities such as contract research, sponsoring of research projects, in-licensing development candidates or buying companies that have assets they need. These activities have always been part of commercial outreach but companies are becoming more overt and explicit in their needs. For example, Merck Sharp Dohme has stated its intention to cap the level of its in-house research activity, specified its requirements and set up dedicated organisations to identify and obtain the capabilities it needs (<http://www.merck.com/licensing/research>).

In the past decade various forms of R&D partnerships have emerged, some stimulated by state intervention and others formed directly between industry and universities (Box 1). One of the earliest examples of these was the Kinase Consortium at University of Dundee, Scotland, initially funded by the Wellcome Trust and Scottish Development Agency and now funded by an industry consortium on a five-yearly basis. This has enabled Dundee University to accumulate a unique and broad ranging platform of drug targets, reagents and know-how relating to protein kinases and phosphatases (www.biodundee.co.uk press release 31 March 2005) [16].

In parallel, public–private partnerships have a significant role to play and are addressing specific issues such as access to drugs for developing countries (<http://www.dfid.gov.uk/pubs/files/ipph-accesspharmaceuticals.pdf>). In the drug discovery space, the Structural Genomics Consortium is funded by government and pharma with the aim of providing protein structures of relevance to human health (<http://www.thesgconline.org/>).

Push and pull

These models may be thought of as 'push', from the owners of IP, and 'pull', from pharma/biotech. Push models arise when IP originators wish to be more effective at translating their research outputs into drug development. They look to create or acquire the capabilities to bridge the innovation gap. Examples of this are Cancer Research Technology and Medical Research Council Technology in the UK, Centre for Drug Research & Development in Canada and the National Institute for Health Roadmap for medical research in the US. In all cases, they focus on commercialising the outputs of their parent organisation or funded components. The funding bodies have started to realise the need to finance such translation—such as the Wellcome Trust Translational Research Awards and Medical Research Council Developmental Pathway Funding Scheme (<http://www.wellcome.ac.uk/>, <http://www.mrc.ac.uk/>). Imperial College London's Drug Discovery Centre is a

BOX 1

Examples of innovative R&D partnering models in drug discovery**Industry/state funded centres****Translational Medicine Research Collaboration (TMRC), Scotland**

The £50 million collaboration comprises four of Scotland's leading universities (Aberdeen, Dundee, Edinburgh and Glasgow), Wyeth Pharmaceuticals, Scottish Enterprise and NHS Scotland Grampian, Greater Glasgow, Lothian and Tayside, and is intended to provide impetus for Scotland to lead the world in the development of personalised medicine, bringing new treatments to patients suffering from a range of serious illnesses. TMRC has already invested almost £8 million to support 28 new research projects covering a wide range of therapeutic areas, including cardiovascular and metabolic disease, the central nervous system, oncology, inflammation and women's health (<http://talentscotland.com>, 10 January 2007).

MédiTech Santé

In July 2005 the French Government's announced its plan to create six world-class 'poles of competitiveness' in a €1.5 billion knowledge transfer initiative, to include the MédiTech Santé health and biotech cluster in Paris and the Lyonbiopole vaccine and diagnostic cluster in the Rhone Valley. Both of these biopharma clusters are supported by companies such as Sanofi Aventis, Servier and GSK (Paris) and BioMérieux, Sanofi-Pasteur, Merial and Du Puy/J&J (Lyon), together with a number of publicly funded research institutions such as the Institut Pasteur, Paris. R&D partnerships are very much a part of these clusters. The overall intent: 'to keep France in the forefront of pharmaceutical innovation and production' (<http://www.scriptnews.com>, 20 July 2005).

Pre-competitive centres**Dundee Kinase Consortium**

The University of Dundee's School of Life Sciences has been partnering with pharmaceutical companies since 1998 in a £20 million+ programme aimed at developing new drugs to fight serious illnesses such as diabetes, rheumatoid arthritis and cancer. The project was initiated to support Wellcome Trust-funded research and Scottish Enterprise-funded commercialisation activity in the laboratory of Professor Sir Philip Cohen, Director of the MRC Protein Phosphorylation Unit. The project has enabled Dundee to accumulate the world's largest collection of drug targets, reagents and know-how relating to protein kinases and phosphatases (<http://www.biodundee.co.uk>, press release, 31 March 2005).

Structural Genomics Consortium

The Structural Genomics Consortium (SGC) was founded in 2003 and is a not-for-profit organisation that aims to determine the three dimensional structures of proteins of medical relevance, and place them in the public domain without restriction. It is funded (\$30 million per annum) by Canada, GSK, Ontario, Merck, Novartis, Sweden, Knut and Alice Wallenberg Foundation and the Wellcome Trust (<http://www.sgc.utoronto.ca/>).

SNP Consortium

The SNP Consortium of pharmaceutical and bioinformatics companies, academic centres and the Wellcome Trust was launched in April 1999 to develop and freely distribute a high-density SNP map of the human genome. The data resulting from this collaboration are to be placed in the public domain, in the form of a relational database that is to be collated, released and maintained by Cold Spring Harbor Laboratory, US (<http://genome.gov/100053>, <http://snp.cshl.org/> and <http://www.sanger.ac.uk/HGP/Poly/snp>).

Corporate mini-labs**Mitsubishi Genetic Therapies Centre at Imperial College**

Initially funded with £10 million over five years to explore potential new areas of medicine.

Sponsored research**GSK's academic Alternative Discovery Initiative at Imperial**

This collaborative research funding framework and alliance management agreement was initiated following introductory meetings between GSK and Imperial College London scientists in 2003. The aim was to increase innovation in GSK's R&D by offering a series of partnering opportunities along selected themes. The framework provides an overarching agreement on IP terms, project costs and alliance management, together with terms of reference for the GSK, scientists identified potential areas of collaboration. Selected project proposals proceeded through the GSK in-house planning process. As a result, GSK is able to tap into the multidisciplinary science base at Imperial, while Imperial receives additional funding and access to know-how for industrial drug discovery.

Proof of concept fund**Johnson & Johnson (J&J)**

J&J have collaborated with Imperial College to create a proof of Concept fund for early stage research. Funding by J&J is matched by Imperial Innovations and potential projects are competitively funded to enable demonstration of Proof of Principle. J&J then have first option to consider further funding of the projects.

London Development Agency (LDA)

The LDA supplemented higher education innovation funding to create a Proof of Concept fund for demonstrating Proof of Principle in early stage translational projects.

State funded**NIH Protein Structure Initiative**

In July 2005, the US National Institutes of Health announced a \$48.5 million award to Structural GenomiX, Inc., and the New York Structural GenomiX Research Consortium to 'produce proteins for structure determination for the collaboration' and provide access to crystallography facilities for its industrial and academic collaborators (<http://www.scriptnews.com>, 8 July 2005).

Scottish Centre for Regenerative Medicine (SCRM) 11/01/2007

A world-leading centre for research into regenerative medicine and stem cells is being built in Edinburgh. Funding support of £24 million from the Scottish Executive will allow the £59 million to be developed by the University of Edinburgh in close collaboration with Scottish Enterprise with an estimated completion date of 2010. The SCRM, which will be part of the new Centre for Biomedical Research at Edinburgh's Little France, will be unique in Europe. In providing state-of-the-art research facilities, manufacturing capacity and commercialisation facilities, the SCRM will have three main elements: High-quality accommodation to support 220 academic researchers, A centre for 'scale-up' development and manufacture of cells and multi-occupancy space to house commercial regenerative medicine research organisations and spin-outs (<http://www.scotland.gov.uk/News/Releases/2007/01/10160831>).

Mixed ventures

See Box 2, academic drug discovery units

BOX 2

Examples of academic drug discovery units (mixed ventures)**Texas Therapeutics Initiative (TTI, The Brown Foundation, Houston, Texas, USA)**

A linked group of Texas-based academic groups addressing drug discovery within the Texas University system. Includes medicinal chemistry, screening, assay development, compound libraries and small molecule and biological therapeutics. Initial areas of focus are neurodegenerative and lung diseases (http://www.uth.tmc.edu/uth_orgs/imm/index.html).

Broad Institute (Cambridge, MA, USA)

A partnership between Massachusetts Institute for Technology, Harvard University and its hospitals and The Whitehead Institute for Biomedical Research. It was established to harness the power of genomics to the benefit of medicine. Includes Harvard Medical School's ICCB-Longwood screening group with extensive compound libraries, chemical biology, computational biology and genomics. It was initially funded by charitable donations of \$200 million and has since attracted funding from Novartis Diabetes Initiative (2004) and RNAi consortium (<http://www.broad.mit.edu>).

Centre for Drug Research and Development (CDRD, UBC, Vancouver)

A Canadian initiative to enable translation of academic drug discovery research across therapeutic areas. CDRD is a non-profit organisation that oversees the activities of the Drug Research Institute(s) (DRI) and Drug Development, Inc. (DDI). Commercial entities will be channelled to the DDI for development. Funded by The Province of British Columbia, a range of charitable foundations and Pfizer research. Includes target identification, drug screening, drug design and synthesis, drug delivery, drug evaluation and project management (<http://www.cdrd.ca/index.html>).

Medical Research Council Technology (MRCT, Mill Hill, UK)

Services projects from MRC-funded research. Includes medicinal chemistry, assay development, screening, compound libraries and therapeutic antibody development (http://www.mrctechnology.org/FI_DDU.htm).

Institute of Cancer Research, Centre for Cancer Therapeutics (ICR, London, UK)

Focuses on cancer therapeutics. Funded by Charities particularly Cancer Research UK. Includes assay development, screening, compound libraries, medicinal chemistry, cancer biology (http://www.icr.ac.uk/research/research_sections/cancer-therapeutics/index.shtml).

Cancer Research Technology (CRT, The Wolfson Institute for Biomedical Research, UCL, London)

CRT translates cancer projects from CRUK research and has medicinal chemists, biochemists, structural biologists, molecular biologists and cell biologists who undertake drug discovery programmes on novel cancer targets in collaboration with academic investigators (http://www.cancertechnology.com/pages/about_devlab_drugdisc.html).

Imperial College Drug Discovery Centre (IDDC, London, UK)

Services projects from within Imperial College London. Initially funded by College Funds and research grants. Virtual biotech-like business plan with core group of industry expertise in medicinal chemistry, computational drug discovery, pharmacology, infrastructure around assay development,

screening and compound library development (<http://www3.imperial.ac.uk/drugdiscovery>).

Dundee Drug Discovery Group, Tropical Diseases Initiative (Dundee, UK)

Specific remit with regard to tropical disease and trypanosomiasis. Funding from The Wellcome Trust and Scottish Enterprise. Includes assay development, screening, analytical and computational chemistry, medicinal chemistry, compound libraries (<http://www.lifesci.dundee.ac.uk/bcdd>).

further enhancement of the push model (<http://www.imperial.ac.uk/drugdiscovery>).

In pull models, pharma companies invest directly into research collaborations to preferentially develop, assess and acquire their early stage outputs. Examples of such investments are Pfizer's funding of the Scripps Institute in the US and Wyeth's funding of a research institute in collaboration with a consortium of Scottish universities (http://www.pfizer.com/research/rd_locations/la_jolla.jsp, <http://www.wyeth.com/news> announced 3rd April 2006).

A hybrid of these approaches can be seen in the creation of consortia of research institutions and companies. For example, the Global Medical Excellence Cluster in the UK brings together key research and commercial players in the South East of England to identify and execute joint research activities more efficiently and more strategically (<http://www.gmecuk.com/>). In all models, the partnering may be based on a combination of capital, infrastructure or material supply.

Academic drug discovery units

The number of examples of academic drug discovery units based within universities is growing, as is the range of capabilities and activities they undertake, from target validation through to candidate approval (Box 2). These are, on the whole, more advanced in the US [26], where universities are more aware of the potential commercial reward from successfully translated projects. In general, these units are focused around a scaled-down pharma model comprising most of the functions required for small molecule drug discovery—including synthetic chemistry, high-throughput screening, absorption, distribution and metabolism analysis.

The UK now has several university or research council-based drug discovery units that are addressing the issues in various different ways but that have a range of the required drug discovery capabilities. The most developed of these are the Medical Research Council Technology Drug Discovery Unit at Mill Hill, London that mainly services MRC-funded projects and has recently implemented medicinal chemistry into its strategy, The Institute of Cancer Research Centre for Cancer Therapeutics and Cancer Research Technology (CRT). Some units focus on specific diseases such as cancer (The Institute of Cancer Research and CRT) and tropical diseases (University of Dundee). Others have broad therapeutic remit (MRCT and Imperial Drug Discovery Centre). As discussed, all have mixed funding models supported by research councils, and research-based charities. Other Universities are focusing on specific aspects of the drug discovery process such as screening and medicinal chemistry at University College London (<http://www.ucl.ac.uk/wibr>) or computational screening at University of Strathclyde (<http://www.ddp.strath.ac.uk/>).

Universities face a number of significant issues when starting an academic drug discovery unit. First, there is the ethical debate about commercialising academic endeavour and the effect on publication strategies. Second, there is the question of the funding model to cover the relatively high costs involved in initiation, equipment purchase and staff recruitment, along with sustainable funding for the long term. There is also, and will continue to be, much debate around the commercialisation of academic endeavour and whether it is appropriate when universities have traditionally been regarded as the home of pure basic research [27]. Despite this – and in order to increase their research funding – most academic institutions now have more commercial strategies, and many have successful technology transfer offices with a portfolio of spin-out companies. Academics are now encouraged to combine research and teaching with collaborations, licensing and spin-out involvement. On the whole, most universities – and Imperial College London is a prime example – operate in the commercial arena to support their continued survival in the modern environment [28,29,30]. These activities are also key to the translation of university-based research innovation to the market.

An often-quoted issue is conflict with regard to publication. Peer reviewed publication is the main metric for academic success and is essential for career progression. So it is crucial to have clear collaboration agreements for academic drug discovery that permit publication of mechanisms, models and disease biology, while allowing essential time for review of patenting potential before valuable intellectual property is disclosed that might compromise a ‘composition of matter’ claim on potential drug candidates.

The mixed (research council, charity and industry) funding models are currently at an early stage and will require sustained commitment in the long term, given the long cycle of drug discovery [31]. Commercial rewards from success in the marketplace may take 10 to 20 years to feed back to basic research, so it is absolutely essential that all parties consider mechanisms to fund the early ‘high-risk’ research.

Links between universities and industry are on the whole poorly developed, and tend to be specific to a project or therapeutic area. That is no accident: the purpose of academic biological and medical research is to pursue innovation and further knowledge about disease, while the purpose of this industry is to develop innovative ideas into therapeutics that address unmet medical needs and grow shareholder value. With the current restructuring of early discovery research and the limited grant funding available, it is both logical and essential that pharma and universities work together. Academia and biotechnology companies will form the ‘front end’ of the drug discovery process, working closely with the pharmaceutical industry to develop therapeutic entities and take these to market.

It will not be easy. Industry and academia have had a difficult relationship in the past owing to different goals, incentives, processes and working practices. Now, though, the drivers to make this mixed model for drug discovery a success (involving academia, biotech and pharma) are compelling to all participants. To make this a success, scientists in academia need to apply industry-standard project management techniques, develop robust assay systems, use standard operating guidelines or procedures, register their compounds and generally ensure high standards of data reporting and control. For its part, scientists in industry need to

allow the room for innovative research to take place without applying their natural control mechanisms too tightly. It is also of paramount importance to develop collaboration models that reward all participants for their success, whether this is achieving milestones in a research project, making discoveries that lead to patent applications, securing follow-on funding for proof of concept or triggering royalty payments. The resulting agreements will not look like those that previously governed more arm’s-length sponsored research at universities.

The Imperial drug discovery model aims to be a true partnership between industry and academia throughout the drug discovery process, utilising the skills and capabilities of each partner rather than reproducing scarce, unique or expensive capabilities and facilities. The Imperial model also recognises that the interaction will be two-way, as pharma has extensive expertise and experience in high-throughput, high-capability drug discovery that is not found with the university system.

We have established that the drug discovery process must continue to evolve and there is a continual need to re-examine and investigate the issues around project attrition (Box 3). There are many hypotheses for declining attrition and suggestions for crucial factors to consider. Academia is ideally placed to consider these hypotheses and develop solutions. In particular, academic–industry partnerships are well placed to develop co-ordinated approaches to target validation and disease linkage in man. Universities with allied clinical facilities are uniquely situated to directly relate projects and targets to clinical questions (for example, identify targets by patient observation, validate these in human systems and identify phenotypic biomarkers) at all stages of what should be an iterative rather than a single linear process to the clinic. Such drug discovery approaches can be optimised by academic–industry partnerships.

Mixed university–industry groups are also able to present new opportunities for drug discovery and development. For example, they are able to address disease groups that are smaller and less commercially attractive (such as antibiotic research, third world diseases and orphan diseases), bring in a range of relevant partners with different expertise and resources from other countries (such as Europe, Asia and the US), funding from non-commercial sources to address recognised issues in the current process (such as the European Union Innovative Medicines Initiative) and, importantly, new innovative environments for the many highly trained pharma scientists made redundant by pharma. For these reasons

BOX 3

Example hypotheses for project attrition and the failure of novel early projects to translate to the market

- Single biological targets not sufficient to achieve efficacy
- Screens that do not reflect efficacy in man
- PK/PD mismatches
- Poor therapeutic indices leading to suboptimal dosing
- Animal disease models misleading
- The continued search for the universal cure-all blockbuster with high/broad market penetration
- Lack of translation of the promise of the genomic revolution
- Focusing on known and validated drug targets rather than novel approaches and so on

we believe that a mixed university and industry research group has the promise of being more innovative and effective at the ‘front end’ of drug discovery than either can be alone.

Conclusions

Drug discovery is difficult, long and expensive. The likelihood of success for any particular project is low, with industry metrics suggesting that around one in 15 projects result in a marketed product [31,32]. Thus, the risks are higher than with most industries; but the rewards can be great: overall, the UK Pharmaceutical industry created a surplus for the UK economy of £4.3 billion in 2007 [33]. Industry’s productivity is declining, however, while costs spiral upwards. This has forced continued re-focusing and restructuring—leading to the development of a new paradigm that involves academia and biotech as the front end of drug discovery, mining and validating novel targets and defining leads and candidates, with pharma as the efficient development machine.

The development of academic drug discovery capabilities cannot be funded solely by the arm’s-length sponsored research models of the past. It requires the structuring of new collaborative models that reward academic contributions with funding, intellectual property ownership and royalty share.

The development of efficient models for academic–industry partnerships in drug discovery, and in particular the mixed model described here for early to late drug discovery, will enable the translation of publicly funded research and the development of novel therapies for developing world, orphan and harder to tackle diseases, support innovative academic disease-related research, support the academic mission and revitalise pharma’s product pipelines.

Academia needs industry. Industry needs academia. It is clear what has to be done: industry, government and research charities need to consider effective strategies to fund and sustain the development of our academic drug discovery capabilities.

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