FORUM
Academy of Medical Sciences

The UK drug discovery landscape

Summary of a joint workshop held on 17 October 2016 by the Academy of Medical Sciences and the Association of the British Pharmaceutical Industry

The Academy of Medical Sciences

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The Academy of Medical Sciences

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The Association of the British Pharmaceutical Industry

The ABPI represents innovative research-based biopharmaceutical companies, large, medium and small, leading an exciting new era of biosciences in the UK. Our industry, a major contributor to the economy of the UK, brings life-saving and life-enhancing medicines to patients. We represent companies supplying more than 80 per cent of all branded medicines used by the NHS, and are researching and developing the majority of the current medicines pipeline, ensuring that the UK remains at the forefront of helping patients prevent and overcome diseases. Globally, our industry is researching and developing more than 7,000 new medicines. The ABPI is recognised by government as the industry body negotiating on behalf of the branded pharmaceutical industry for statutory consultation requirements including the pricing scheme for medicines in the UK.

All web references were accessed in November 2016.

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FORUM workshop, October 2016

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Executive summary

Over the past decade, the global process of drug discovery has shifted, becoming more open and collaborative across both disciplines and sectors. The UK must consider how it can best respond to these changes to support and facilitate growth for the UK within this shifting drug discovery landscape

The UK has an outstanding track record for the research and development (R&D) of new medicines, built upon a vibrant and diverse life sciences ecosystem. With the significant changes taking place in R&D and healthcare globally, the drug discovery landscape in the UK has also evolved to meet these changes. The Association of the British Pharmaceutical Industry (ABPI) report on 'The changing UK drug discovery landscape' provides an evidence base for the changing nature of preclinical drug discovery in the UK.[1]

The Academy of Medical Sciences and the ABPI held a FORUM workshop on 17 October 2016 on 'The UK drug discovery landscape' with stakeholders drawn from across the life sciences sector. The workshop sought to explore, in-depth, the changes taking place in the drug discovery landscape over the past decade, and how the UK can build on its strengths and overcome current and future challenges to maintain leadership in R&D, in the light of a broader UK life sciences industrial strategy. Areas identified as key to enhancing the drug discovery landscape in the UK included:

- Continuing to **facilitate cross-sector collaboration and outsourcing** in drug discovery to foster open innovation, including through long-term collaborative arrangements such as public-private partnerships. In addition, driving more integrated working across industry and academia to piece together the drug development pathway.
- Fully **integrating the NHS into the broader drug discovery environment**, with greater patient and clinician engagement, to **improve the use of health data and clinical infrastructure** for innovative drug discovery. In addition,

[1] The Association of the British Pharmaceutical Industry (2016). *The changing UK drug discovery landscape.* www.abpi.org.uk/our-work/library/industry/Documents/the-changing-UK-drug-discovery-landscape.pdf

it is important to ensure that the NHS – and subsequently the UK – delivers uptake and adoption of such innovations when they are developed.

- Enhancing the funding landscape for discovery in the UK, including **attracting more international funding and venture capital** through raising awareness of the international opportunities available and promoting the discovery strengths of the UK life sciences ecosystem, particularly in the light of Brexit. Funding for discovery activities also increasingly needs to move towards more flexible, long-term commitments.
- **Building capacity and capability** across sectors and **ensuring the sustainability of the pipeline of scientific and leadership skills** in the next generation of drug discovery scientists and life science entrepreneurs, particularly given the downsizing of in-house drug discovery in large pharmaceutical companies. Therefore horizon scanning is needed to identify potential future skills gaps. In addition, a multidisciplinary approach is fundamental to discovery science, and mobility and training across different sectors supports development of the necessary skill set and experience for drug discovery leadership.
- **Continuing to enhance the research base in the UK** through supporting new approaches and technologies for drug discovery and capitalising on the potential of informatics. Increasing the robustness and efficiency of such research will help to de-risk the wider R&D process and support continued UK leadership in innovative technologies.
- Propagating a **culture change across the life sciences ecosystem** to align – and create a better understanding of – expectations and scientific practices across sectors. This includes exploring ways to address and mitigate risk in the discovery process, clear communication on definitions and expectations for target identification and validation and data reproducibility, and moving to focus on impact and translation of academic research.
- Recognising the **importance of a diverse drug discovery ecosystem** and the key role that each sector plays in contributing to the life sciences landscape.
- Establishing and **collecting metrics to be able to evaluate further developments** in the UK drug discovery landscape.

Introduction

The UK has a strong history of innovation in drug discovery. From Alexander Fleming's discovery of antibiotics to development of monoclonal antibody treatments, UK drug discovery has contributed to huge improvements in medicines development and healthcare. With the evolution of the drug discovery landscape at both a UK and global level, it is important to ensure that the UK can continue to respond to this rapidly changing environment.

The strengths of UK drug discovery are founded on a complex landscape of excellence across academia, industry and the national healthcare system (NHS). As noted by Professor Herbie Newell FMedSci, co-chair of the workshop on 'The UK drug discovery landscape', the UK punches well above its weight in academic success proportional to both funding and population size. In addition, the biopharmaceutical industry is the largest investor in research and development (R&D) in the UK, and the UK has notable strengths in its single national healthcare system, and patient and public engagement.[2] Together, this landscape should provide the expertise, resources and culture to reach the critical mass necessary for truly innovative biomedical research that bridges the translational gap, and there is an opportunity to capitalise on these strengths to ensure that the UK remains at the forefront of global R&D.

Approaches to preclinical drug discovery are changing with a shift to more collaborative and open models as part of the overall process, combined with an increasing recognition of the scientific complexity of disease and need for stratification. This is embedded within the wider context of shifting patient demographics and rising burdens on healthcare systems such as constrained healthcare budgets and changing commercial environments. These changes

[2] Association of the British Pharmaceutical Industry (2016). *Open for Innovation: UK Biopharma R&D Sourcebook 2016.* http://www.abpi.org.uk/our-work/library/industry/Documents/Open_for_innovation_ABPI_Sourcebook_2016.pdf

bring new challenges for the UK within the global setting; to adapt and respond to ensure the future sustainability of the drug discovery process including its workforce. A cross-sector, multidisciplinary approach will be essential to addressing such challenges. A recent report commissioned by the ABPI illustrated these changes in the preclinical drug discovery landscape, providing an evidence base to underpin future approaches and policy decisions.[3]

Therefore, on 17 October 2016, the Academy and the ABPI convened a FORUM workshop on 'The UK drug discovery landscape', building upon previous discussions from a meeting held by the Wellcome Trust and the Medical Research Council on the academic and funders' perspective of drug discovery in the UK. The workshop brought together key stakeholders from across industry, academia, charities, regulatory bodies and Government, amongst others, to explore the findings of the ABPI report and identify challenges and ways forward for drug discovery in the UK. The morning session comprised scene-setting presentations from different stakeholders on their perspectives of the drug discovery landscape which can be found within Annex 1.These presentations were followed by in-depth discussions in the afternoon focused on some of the key themes from the ABPI report and the body of this report explores these emerging themes and proposed next steps from the meeting. The participant list is in Annex 2 and the meeting agenda in Annex 3.

We would like to thank Professor Herbie Newell FMedSci, Emeritus Professor of Cancer Therapeutics at Newcastle University, and Dr Neil Weir, Senior Vice President of Discovery at UCB, for co-chairing the event, and the speakers and participants for their active contributions throughout the meeting.

[3] The Association of the British Pharmaceutical Industry (2016). *The changing UK drug discovery landscape.* www.abpi.org.uk/our-work/library/industry/Documents/the-changing-UK-drug-discovery-landscape.pdf

Enhancing the UK drug discovery landscape

Over the past decade, the UK drug discovery landscape has experienced a shift towards a more a collaborative model across both sectors and disciplines; increasing adoption of open innovation and new funding approaches; developments in technological and scientific capabilities; and a drive towards a more patient-centric approach. Delegates discussed the importance of integrating drug discovery into a broader industrial strategy for the life sciences, and explored ways to build upon the current environment to ensure that the UK maintains its world-leading offering in drug discovery.

Collaboration

Collaboration and open innovation are becoming increasingly important in the UK drug discovery ecosystem, which is increasingly moving towards a partnership, outsourced approach for access to expertise and better integration across sectors. This is demonstrated by the rapid expansion of the contract research organisation (CRO) sector and growing number of cross-sector collaborations in the UK. Delegates discussed how the UK environment could further support and facilitate such a networked approach to drug discovery.

Open innovation frameworks

Delegates discussed the benefits of an open interface across organisations and sectors to facilitate innovative approaches to drug discovery and sharing of data, resources and expertise on both a national and international level. Large-scale open innovation centres were seen to play an important role in supporting open innovation by decreasing the 'activation energy' for collaboration, and by bringing together scientists from different organisations or groups in physical proximity. For example, at the Francis Crick Institute the laboratories are arranged to facilitate interaction of scientists between research groups, including between academic and industry groups, which is expected to facilitate sharing of scientific data and ideas as well as provide opportunities for skills development. Another example of an innovative model is the UCB Technology Platform Access Programme for antibody discovery where UCB has partnered with the Medical Research Council to enable scientists to work in collaboration with industry and use the company's antibody platform capabilities.[4] However, the potential risk for open innovation centres to become closed in themselves, and the need for them to remain open to further interaction across the national and international landscape, was highlighted.

Public-private partnerships (PPP) are increasingly used as long-term collaborative arrangements across sectors and it was confirmed that these play an important role in managing high risk research through distributing risk across multiple partners and sectors. In addition, it was considered that PPPs offer a particular opportunity in underfunded disease areas where a temporary bridge between blue sky, not-for-profit and industry research may drive renewed drug discovery success. For example, it was proposed that this model could be useful in dementia to overcome recent lack of progress (which has reduced confidence and funding) by demonstrating market potential. The Structural Genomics Consortium (SGC) and the TB Alliance have used the PPP model highly successfully in this way, to catalyse research through partnerships across sectors.[5]

The Innovative Medicines Initiative (IMI), the world's largest medical research PPP funded jointly by the European Commission and the European Federation of Pharmaceutical Industries and Associations, was discussed as a key mechanism which has supported international and cross-sectoral collaboration in Europe. It was highlighted that a focus on funding streams and initiatives which incentivise and support international collaboration should be maintained following Brexit.

Some delegates considered whether the impact and efficiency of drug discovery could be maximised by focusing on the different strengths of individual sectors along the pathway; for example, whether academia should focus on strengths in fundamental discovery science and industry on development research. However, it was argued that despite a need to understand key strengths and maximise these, different sectors bring complementary expertise along the discovery and development pathway. Therefore rather than fragmenting the pathway, equipping all sectors with a better understanding of the whole process and their role within this would support effective collaboration and strengthen discovery pathways. In addition, while there has been an expansion of smaller organisations and CROs, there has also been a reduction in the numbers of scientists working in larger biopharmaceutical organisations. This reduction has released highly trained expertise into smaller start-ups and PPPs but is more a 'one off' skill injection rather than a steady state source of these skills. This potential sustainability challenge is covered under 'Building capacity and capability'.

[4] www.mrc.ac.uk/news/browse/mrc-and-ucb-join-forces-to-offer-access-to-ucb-s-novel-antibody-discovery-platform/
[5] www.tballiance.org/

Case study: SGC public-private partnership

The Structural Genomics Consortium (SGC) is a highly successful not-for-profit PPP model for advancing drug discovery science, specifically in less well-studied areas of the genome.[6] An international network of academia, industry and charitable organisations, amongst others, works collaboratively as part of the SGC to characterise selected target proteins of biomedical importance. Any data generated on these targets as part of the consortium is made publically available through an open source approach, which enables widespread dissemination of the science to facilitate drug discovery research. Notably, some of the findings from the SGC have included elucidating the structure and functional characterisation of TNIK protein, a schizophrenia target, as well as characterisation of various potential drug targets such as methyl-lysine binding proteins with potential relevance to cell reprogramming and regenerative medicine.

Driving open innovation through data sharing

Delegates explored how data sharing can facilitate innovation, and the challenges of managing Intellectual Property (IP) effectively and appropriately in an open drug discovery landscape. Concern was expressed that over-protection of raw data – which may not be as valuable as perceived – can cordon off areas of disease research, and there is a need to protect against such data wastage. Some delegates held the opinion that IP arises from how information on a target is used, rather than which targets are being researched. Therefore it was proposed that one possible mechanism to reduce unnecessary duplication of research could be to establish a mechanism by which the vast amounts of early biological data collected on 'failed' drugs or de-validated targets can be made available.

It was also suggested that a top-level repository could be established to share targets which are being, or have been, studied. A 'pay to play' model (contributing data in order to be able to use the resource) could incentivise participation, and further consideration would need to be given to appropriate design and incentives to facilitate the participation of different sectors (academia, industry etc,). Delegates suggested that this model could be first piloted amongst academia and then opened to the wider life sciences ecosystem as appropriate. The repository could build a knowledge sharing platform for drug discovery, with significant efficiency savings through preventing unnecessary duplication of research and facilitating the identification of collaborative opportunities in areas of mutual interest. This wider forum could be based upon the open source, pre-competitive model used at the SGC.

There are several important existing repositories of patient data, the most notable of which is the NHS itself alongside other large data resources such as the UK Biobank and the Francis Crick Institute. Delegates noted, in particular, the value of linking genomic and other 'omic' data and clinical phenotypic data. Linkage between NHS and other data repositories could capitalise on this potential but will require better standardisation of data capture, storage and sharing practices. It was advised that enhancing data sharing and linkage systems and making them accessible for testing medicines on a global level could attract global investment, and implementing such a data sharing ecosystem presents a real opportunity for the UK.

Integration with the NHS

As a single centralised healthcare system the NHS offers a unique ecosystem to support clinical target identification

[6] www.thesgc.org/

and validation through building a rich repository of patient data and opportunities for experimental and translational medicine. It could thus be a significant attraction for global investment in the UK.

There is potential for better integration of the NHS within the broader discovery landscape, which would ensure that drug discovery is fully aligned to patient and clinician needs. Despite the NHS acting as one overarching system, it is comprised of many fragmented components that could be better linked to facilitate collaboration, particularly with global companies who may be less familiar with the structure of the UK health system. This should build on the work of the National Institute for Health Research Biomedical Research Centres (BRCs) and Translational Research Partnerships and Collaborations, which offer particular opportunities for translational and experimental medicine and target validation, and could be further integrated into their local drug discovery landscape through collaborations and regular interactions.

Delegates illustrated the importance of NHS patient data for directing drug discovery and reducing R&D failure by enabling stratification of patients and disease, identification and verification of targets, development of biomarkers (or surrogate markers) for further stratification, proof of mechanism and later, proof of concept. The use of NHS data raises important challenges surrounding data governance and consent and it is important that stakeholders from across the drug discovery landscape engage with public discussions and concerns to facilitate the appropriate use of patient data in medical research. It was suggested that the population sequencing initiatives in Iceland could be used as exemplars for achieving this engagement.[7]

Involvement of clinicians and patients in early drug discovery is vital for shaping R&D. Greater awareness and understanding of the drug discovery process, and how this is changing, would support integration of the NHS into the drug discovery landscape and facilitate target validation through clinical collaborations. It was suggested that for clinicians and other healthcare professionals, education around drug discovery should be integrated into training at every level. In addition, clinician understanding could be furthered through industrial work placements, targeting both early career medics and clinical academics and lecturers using 'out-of-programme' opportunities to do industrial placements. It was determined that rigidity in clinical training requirements and associated timescales currently restricts such opportunities. However, with a single training system for clinicians, the UK is well-placed to introduce more flexibility and incentives into training to encourage collaboration and involvement in drug discovery. Again, this could build on and extend the engagement currently facilitated via the BRCs.

Opportunities

- Encourage open innovation practices and collaborative ways of working across sectors through: sharing best practice and examples of success; increasing awareness of existing platforms and opportunities to engage; facilitating relationship building to enable the development of new opportunities; and considering opportunities for new open innovation and interdisciplinary platforms.
- Consider establishing a pre-competitive data sharing forum for sharing drug discovery data. For example, this might list who is working on different targets and could first be piloted amongst academia.
- A long-term approach to better integrate NHS staff and patients in early drug discovery is needed, building on the work of the BRCs. For example, further training on drug discovery and development for healthcare professionals, opportunities to contribute to discovery research, or training/placement schemes with industry, could be developed.

[7] Gudbjartsson DF, *et al.* (2015). *Large-scale whole-genome sequencing of the Icelandic population.* Nature Genetics **47**, 435-444

Funding Models

There is a vibrant funding landscape for drug discovery in the UK with significant investment particularly in early discovery activities. However, participants felt that proportionally there is less venture capital investment and diversity of funding opportunities for drug discovery in the UK than for its main competitor, the US. Therefore delegates agreed on the need to attract more private investment to the UK as well as developing alternative models for better using existing funding to fill this gap.

Private and market finance

Venture capital (VC) is an important source of funding for biotech companies in the US and offers potential for expanding large-scale investment in the UK. This is particularly pertinent for small and medium sized enterprises (SMEs) which are sometimes required to provide ever increasing levels of drug/target data before large pharmaceutical companies take research forward. VC investment in drug discovery requires long-term financial commitment and delegates agreed that, whilst increases in VC fund availability have been seen in the UK in recent years, proactive measures should be taken to attract and grow this funding in, and from outside of, the UK. The importance of public funding in the form of the Biomedical Catalyst was also highlighted, and the continuation of this scheme was welcomed.

A further challenge to biotechs accessing finance in the UK is the lack of a sustainable UK public market when compared to the offerings available in the US. This can be a barrier to the public listing of companies, which limits the options for growth for UK biotechs and their investors. This may drive the strategy of biotechs in the UK towards selling assets, limiting their growth and development into medium-sized companies. In contrast, easy access to public markets in the US provides companies with more straightforward options to either list or sell.

International funding streams

The UK drug discovery landscape competes effectively at a global level, attracting and maintaining significant R&D investment from global biopharmaceutical companies as well as large scale overseas investment including private financing and grants from sources such as the National Institutes of Health, which provide important revenue and increase international profiles for biotech and CROs. It was argued that academic and small company researchers would benefit from a better understanding of the potential international funding opportunities available, which could help them to attract further international funding.

On the other hand, the complex drug discovery landscape in the UK can be challenging to navigate for non-UK organisations and so delegates indicated support for a national database or 'map' of discovery work in the UK, which could facilitate entry and interaction with the UK drug discovery landscape for overseas investors and funders The Knowledge Transfer Network have produced a UK Medicines Discovery UK Landscape interactive tool which provides a useful starting point.[8] Although the usefulness of such a one stop shop was recognised, it was cautioned that previous attempts to develop such a resource have stalled and that it would quickly become out-of-date without constant monitoring.

In addition, delegates cited the importance of EU funding streams for discovery research such as IMI and the Seventh Framework Programme (FP7) as well as investment streams for small companies such as from the European Investment Bank. Delegates welcomed the Government's commitment to ensure continued funding for any ongoing EU projects beyond the UK's departure from the EU, but reiterated the need to maintain access, or build sustainable investment of similar value, to ensure continuation of these activities beyond this time.

[8] http://mdlandscape.ktn-uk.org/

Changing grant structures

Delegates proposed that a proportion of research grants should reflect the changing discovery landscape with a shift towards longer-term, more flexible programmatic commitments such as consortia-based arrangements, to mirror the length of time and adaptability required for drug discovery rather than smaller, project-based grants. It was noted that this would not only encourage investment in innovation and reduce administrative burdens but would also facilitate the recruitment and retention of the best scientific talent. In addition, delegates described the need to define long-term translational aims in grant applications as challenging for some early research and there needs to be sufficient flexibility to balance these needs with academic strengths in basic science. Grant funding structured around a portfolio of research was proposed as a valuable alternative to short-term funding streams and this flexible portfolio approach is implemented at the Francis Crick Institute, enabling researchers to move between projects and pursue the most promising science. Finally, it was proposed that changing grants for biotech and CRO start-ups to increase availability of initial funding would support company growth, better facilitating sustainability by avoiding the current 'pay as you go' approach.

Opportunities

- Building a better understanding of international funding opportunities amongst the UK drug discovery stakeholders, complemented by providing a clearer picture of the UK ecosystem for international funders through open innovation events and relationship building.
- Call on Government to ensure sustainable funding for drug discovery including collaborative work, particularly in the context of any funding changes following the UK's departure from the EU.
- Propagating a culture change in funding for discovery activities to establish more flexible, long-term financial and resource commitments.

Building capacity and capability

Skills development – building a sustainable workforce

With the shift away from in-house activity in pharmaceutical companies towards an increasingly outsourced and collaborative approach, there is a risk that there may be significant skills gaps in drug discovery in the future. Indeed, skills gaps are already being reported. In particular, skills identified as difficult to recruit included those in complex *in-vivo* disease models; translational clinicians and experimental medicine; medicinal chemists; informaticians; data scientists; and DMPK skills.[9] Overall, there is a lack of clarity across sectors about the skills and training routes available to fill these gaps and it was proposed that establishing a standard minimum level of competence would facilitate recruitment of expertise needed for drug discovery. It was suggested that there is a role for learned societies in supporting the development of these skills, such as the work of the British Pharmacological Society in addressing areas such as *in-vivo* training.

As well as identifying current skill gaps, it is vital to anticipate the skills needed by the next generation of drug discovery scientists (both scientific and 'softer' skills). The importance of ensuring the sustainability of this future

[9] The Association of the British Pharmaceutical Industry (2015). *Bridging the skills gap in the biopharmaceutical industry.* www.abpi.org.uk/our-work/library/industry/Documents/Skills_Gap_Industry.pdf

repertoire of skills was expressed, as whilst skills such as medicinal chemistry are currently found in academic drug discovery units, biotech and CROs, much of this workforce was originally trained in large companies who now have less in-house capacity in the UK. In the future pipeline, a broader range of partners may be needed. However, there were also concerns about whether there is sufficient resource and stability within SMEs and CROs to nurture and train such researchers across the breadth and depth of drug discovery, and in drug discovery leadership and decision making. A possible solution suggested was partnering of biotechs to create sustainable clusters able to support shared training placements for scientists to learn both scientific and project management/leadership skills. Universities will also play a key role in delivering high-quality scientific discovery training.

Delegates emphasised that ensuring access to international talent is central to maintaining a high quality and diverse skill set in drug discovery in the UK and, in the light of Brexit, it is important to ensure that the UK can continue to recruit, and engage with, the best talent from abroad.

Fostering cross-sector discovery skills

There was strong agreement that the drug discovery ecosystem in the UK is underpinned by an outstanding academic research base, and delegates emphasised the need to continue building on this through long-term strategy and investment. In addition, the importance of supporting and enabling academia to deliver discovery activities– in some cases – to industry standards was emphasised. The value of industrial placements and internships in developing such scientific capabilities alongside softer skills such as leadership and entrepreneurship was discussed. Although there are a variety of frameworks to build these skills, it was suggested that this may be a gap where biotechs or CROs could be supported and incentivised to offer more such placements. Delegates explored specific opportunities for developing skills along the career pathway:

- Strong support was voiced for undergraduate sandwich placements in industry. Apprenticeships may also become a more important component of industrial skills development, especially for graduate level apprenticeships. It was felt that companies should be made more aware of the apprentice levy and how to best use it to fill the skills gap.[10]
- For PhD students there was support for mirroring initiatives such as CaSE studentships which provide experience of, and training to, industry standards and ways of working.[11] It was noted that even longer periods of experience in industry with a view to more long-term mobility would be valuable.
- Long-term collaborative initiatives between individual companies and academic institutions also offer significant scope for industrial investment in capability building. For example, the North West Centre for Advanced Drug Delivery, a partnership between AstraZeneca and the University of Manchester, facilitates close collaboration between academic researchers and industry scientists, and the University of Oxford's Doctoral Training Centre offers opportunities for joint industry-academia collaborative projects across various industry partners.[12,13]
- At later career stages, concern was expressed about the lack of industry engagement with post-doctoral researchers. Delegates argued that this has occurred largely due to the academic training structure alongside a lack of career advice for early career researchers. This could be avoided by early industry engagement on career options and through effective networking. In addition, delegates highlighted the benefits of mentoring schemes involving senior scientists with experience from across sectors, and initiatives such as the Young Entrepreneurs Scheme which are responding to the need for 'soft' skills.[14]

Sector permeability and mobility

There was consensus on the benefits of improving long-term bilateral permeability between sectors at all career stages to foster shared language as well as skills and knowledge that enhance drug discovery and drive further collaboration. Overall, the need for a more mature interface between sectors was recognised to develop the discovery

[10] The apprentice levy requires all employers operating in the UK with a pay bill over £3 million each year to invest in apprenticeships. The levy will reflect 0.5% of an employer's annual pay bill and must be spent within 18 months.
www.gov.uk/government/publications/apprenticeship-levy-how-it-will-work/apprenticeship-levy-how-it-will-work
[11] www.bbsrc.ac.uk/skills/investing-doctoral-training/case-studentships/
[12] http://research.bmh.manchester.ac.uk/nowcadd/
[13] www.dtc.ox.ac.uk/
[14] www.biotechnologyyes.co.uk/biotechnologyyes/index.aspx

workforce, and it was suggested that it would be useful for industry to continue to shift away from piecemeal funding and inflexible grants, with academia moving towards more standardised training and work practices. Some of the barriers to permeability across sectors can be overcome through a wider culture change as described later.

It was suggested that mobility schemes can be built on initiatives such as the Immunology Catalyst at GSK which enables academic immunologists to work at GSK alongside industry scientists, allowing access to GSK's platforms whilst retaining ownership of IP and enabling the scientists to return to their institutions after a few years.[15] Institutes such as the Francis Crick have similar interchangeable arrangements for both industry and academic researchers. Secondments and networking opportunities also allow established researchers to permeate new sectors and, crucially, bring back knowledge and experience upon reintegration. For those earlier in their careers, the benefits of co-supervision of PhD students by both academia and industry representatives was described, potentially through the expansion of models such as the Royal Society Industry Fellowships which facilitate collaborative projects across industry and academia. More permanently, it was highlighted that there should be clear routes by which industry experts can enter academia and for academic professors to enter industry through joint appointments or as visiting lecturers/advisers. Changes in academic and industrial culture, and understanding of the two, will strongly support such mobility as well as collaboration, as discussed further below.

Case study: Stevenage Bioscience Catalyst

The Stevenage Bioscience Catalyst is a successful example of promoting sector permeability in a bilateral manner. It is an open innovation bioscience campus jointly supported by the Department for Business, Energy and Industrial Strategy, GlaxoSmithKline, Wellcome Trust and Innovate UK.[16] The campus aims to accelerate advances in biomedical discovery through building a collaborative environment across academia, pharmaceutical, biotech and diagnostic companies amongst others. It has been designed to facilitate co-operation and dialogue between scientists with availability of platforms and expertise to support scientific discovery, and tenants retain full independence and ownership of IP generated.

The importance of multidisciplinarity

Delegates recognised the importance of a multidisciplinary approach for drug discovery and translation of research with opportunities to better integrate mathematicians, bioinformaticians, computer scientists, physicists and others with traditional bioscience and discovery disciplines. It was noted that UK Research and Innovation (UKRI) could help to facilitate this multidisciplinary approach through drawing together the Research Councils and provides an opportunity for developing alternative models of funding across different disciplines.

It was widely agreed that experience of the multidisciplinary nature of drug discovery needed for skills development was driven through areas of critical mass whether in academia, industry or charity. To create this critical mass in industry, with a reduced number of major pharmaceutical companies, biotech companies must be better supported to ensure that they can provide multidisciplinary experience and training for in-house scientists, potentially through the cluster system mentioned previously. Additionally, biotech and CROs may be able to consolidate skills through membership of schemes such as the Science Industry Partnership. In particular, research centres were also discussed

[15] www.gsk.com/en-gb/careers/areas-of-opportunity/research-and-development/immunology-catalyst/
[16] www.stevenagecatalyst.com/

as useful and sustainable collaborative models for building critical mass of finance, people and technology, often accompanied by close integration with hospitals and associated healthcare professionals. The Institute of Cancer Research was held up as an example of where scientists can access the same type of multidisciplinary training offered in industry. However, it was also cautioned that through building such critical mass and self-sustainability, these institutes can risk becoming insular and difficult to access and care should be taken to continue to ensure a collaborative environment.

Opportunities

- Horizon scanning to identify future skills gaps and ways to address these to ensure the sustainability of the skills repertoire in the context of the Industrial Strategy. This includes ensuring continued access to global talent in the light of Brexit.
- Developing training pathways to support 'soft skills' such as leadership and decision-making skills, as well as technical and scientific skills, to support both drug discovery scientists and the next generation of entrepreneurs.
- Ensuring a collective approach to increasing bilateral permeability between sectors.
- Increased support to enable biotechs and CROs to offer training and experience for students and both early career and established researchers, potentially through the development of training clusters.

Underpinning the science

The UK is considered to excel in early biomedical research which attracts substantial financial investment. There was widespread consensus on the importance of ensuring that drug discovery is integrated into a broader life sciences Industrial Strategy, to build strategically on the UK's historical leadership in drug discovery. Delegates explored steps to further enhance discovery science in the UK, and ways of 'de-risking' the drug discovery process through capitalising on emerging technologies and increasing the robustness of research. With limited funding available, the possibility of prioritising UK leadership in certain areas of drug discovery and the best ways to accelerate drug discovery were discussed.

Refining and de-risking the science: target identification and validation

Robust target identification and validation is critical to ensuring that the right target is selected –and helping to 'de-risk' the R&D process – requiring an in-depth understanding of both the disease and patient stratification. Overall, improving the quality of targets and subsequent compounds entering clinical development, and developing robust biomarkers in parallel for 'go' or 'no go' decisions, offers efficiency gains in R&D by reducing the number of failures seen in clinical trials. However, delegates noted that there are often key differences between industry and academia definitions and expectations for target validation. A strong need to establish common definitions and standard practice for target identification and validation across sectors was identified to tackle variation seen in current practice and facilitate effective collaboration, and this is addressed in the section on 'Culture change'.

Delegates noted the significant potential to maximise on expanding capabilities in informatics to enable intelligent use of data for improvements to drug design and target validation – again helping to de-risk drug development at an early stage. It was noted that these models will be highly complex to develop and will need to be carefully optimised to ensure that models provide added value. Conversely, there was some debate around realistic expectations for this technology, with one delegate highlighting that it still cannot be used, for example, to predict reliably, the affinity of a small molecule for a drug target, and so predicting interactions in more complex systems in the near future may not

be possible.

Variation in data reproducibility was reported as a notable challenge. Reasons given for this problem ranged from technical aspects such as using non-standard assays and the use of sub-optimal tool compounds, to wide scale differences in training and work practices, and these issues are explored in detail in the Academy's report on research reproducibility.[17] It was highlighted that challenges around reproducibility involve academia and industry, and again there may be differences in perceptions between sectors. Connecting universities to biotechs was one suggestion to help create culture change in this area, and in general it was felt that collaborative frameworks should ensure clear definitions around the data that are required and the route to acquiring these.

Drug modality and combination therapy

An opportunity was identified for the UK to capitalise on advances in diversification of drug modalities and delivery technology and one delegate advised the importance of academic funding for developing such new modalities (such as that through the SGC). As seen with monoclonal antibodies, modalities can develop rapidly and become underpinning and disruptive technologies, and so participants emphasised the importance of continuous horizon scanning and flexible funding so that the environment is prepared to accommodate these novel modalities. Best practice examples of research centres that have responded to this need in a non-risk averse, 'adventurous' manner could encourage others to follow, and new ventures such as the Medicines Discovery Catapult are important resources for furthering such technology.

There is increasing opportunity to mix multiple different therapeutic modalities as part of combination treatments. However, it was suggested that there can be a lack of economic incentive for creating these combination approaches, particularly where no single company owns all of the components. Therefore consideration needs to be given as to how these types of combination therapies are valued, and a combination approach could be supported through more collaboration and pre-competitive partnerships.

Case study: Cell and Gene Therapy Catapult

The Cell and Gene Therapy Catapult, supported by Innovate UK, is one way in which new modalities in drug discovery have been supported and de-risked in the UK, and it will be important to continue to horizon scan for further such opportunities in the future. The Catapult has expert in-house capabilities, infrastructure and technologies designed to address the unique challenges of cell and gene therapies across the lifecycle from early discovery through to market access.[18] It aims to find innovative ways to ensure these processes are efficient, robust and targeted to clinical need and the specialised skill base is particularly useful in an area with such complex and wide-ranging manufacturing processes. A recent example of its partnership work is development of a novel point-of-care benchtop thawing system for cell-based therapies in collaboration with Asymptote. Cell-based therapies are cryopreserved and careful thawing of these products at clinical sites is critical for administration. Therefore development of an easy to use, fit-for-purpose certified thawing system

[17] Academy of Medical Sciences (2015). *Reproducibility and reliability of biomedical research: improving research practice.* www.acmedsci.ac.uk/download.php?f=file&i=32558

[18] www.ct.catapult.org.uk/about-us

compliant with Good Manufacturing Practice would help to overcome some of the barriers to commercialisation of cell therapies.

Developing a scientific strategy

A recurring theme over the course of the day was whether a more strategic approach should be taken to prioritising investment in specific areas of drug discovery in the UK whether in selected disease areas, treatment modalities or technology. For example, it was agreed that certain disease areas would benefit from focused funding as demonstrated in oncology research. However, it was strongly questioned whether such restrictions on investment in drug discovery would benefit the wider ecosystem and there was disagreement as to whether funding should be focused in this way or if it would be better used to provide multiple funding and collaborative opportunities across many therapy areas and stages of the R&D process. It was also suggested that there should first be a focus on operating as part of the global ecosystem, with the opportunity to develop specific areas for attracting investment. In addition, it was stressed that a future strategy should recognise that drug discovery is not a single linear pathway but consists of multiple separate stages.

Opportunities

- Drug discovery should be integrated as a key component of a broader life sciences Industrial Strategy, with appropriate investment to promote continued UK leadership in this space.
- Horizon scanning and flexible funding for new modalities is needed to allow the UK to capitalise quickly on emerging technologies.
- A potential framework for developing combination therapies should be explored, with appropriate incentives in place for creating such products. This would require engagement of the life sciences sector with health technology assessment bodies, payers and commissioners.
- Clear communication and guidelines on data use and requirements for data reproducibility are needed across sectors.

Culture change

Delegates explored the need to better understand expectations across sectors for drug discovery and the importance of overcoming ingrained perceptions of different sectors which may impede open innovation and collaboration.

Differences in scientific practices

Differences in expectations between industry and academia at various stages of drug discovery were identified as a challenge. There is an overarching need to ensure clear communication and understanding of the needs and expectations of all partners involved in drug discovery, and collaboration between sectors will help to foster an understanding of these expectations. One key challenge highlighted was a mismatch in understanding of what constitutes target validation. As one example, with a move towards stratified medicine, industry increasingly expects

that this not only identifies if a target valid but also the patient sub-populations in which it is relevant. However, there was debate as to whether academia could realistically deliver to these demands and it may depend on the funding available to do so. Some of the routes to support mobility and permeability between sectors, discussed above, could support improved mutual understanding.

Perceptions across sectors

It was highlighted that many of the perceived cultural barriers to industry-academic partnerships are often misconceptions on either side. Competing interests around publication – with academic pressures to publish propagated by incentives such as the Research Excellence Framework (REF) and industry priorities to protect commercial IP – were cited as one of these barriers to partnership. However, it was stressed that this should be less of a concern as industry scientists are also able, and indeed often encouraged, to publish much of their research. Delegates also supported a shift to focus on impact and other assessments of academic discovery output, as introduced in the 2014 REF and similar to the culture fostered at MIT, rather than using solely income and publication record. It was suggested that a culture of valuing impact needs to be propagated not only in academic funding and research but also in Technology Transfer Offices.

Alongside improvements to industry-academia perceptions, there was also a call to improve understanding of the rationale behind regulatory requirements. Whilst some specific regulatory requirements were viewed as a barrier to bringing new drugs to market, it was widely felt that there may be a poor understanding of the importance of most of these regulatory measures and the full scope of considerations that regulatory bodies must account for. Finally, it was noted that public engagement with the drug discovery process should be improved. Increased engagement at all levels of drug discovery will help to focus research and could improve patient participation in research, including through use of their health data. Potential mistrust, particularly of industry drug discovery, must be challenged and this could be driven by a transparent approach to research that would encourage trust and participation.[19] This is a concept explained in the Academy's project on 'How can we all best use evidence' which is, in part, exploring public perceptions of scientific evidence including a workshop on conflicts of interest and a public dialogue event.[20]

Managing risk

Throughout the discussions, delegates referred to the high levels of risk involved in early drug discovery. It was stressed that compared with the UK a culture has been created in the US where there is less '*fear of failure*', although it was noted this may also relate to availability of funding. Some delegates cautioned that industry, in particular, can be perceived as highly risk averse. However others noted that, for industry scientists themselves, the responsibility and risks are vast when making 'go' or 'no go' decisions on progressing a drug to the next stage of development. A deeper understanding of the molecular basis of disease, more robust target validation, patient stratification and the availability of more effective biomarkers will help to reduce some of this risk through enabling clearer, well-informed decisions.

Maintaining a vibrant ecosystem

In general, delegates acknowledged the importance of the heterogeneity of the ecosystem and the key roles of each sector within this landscape. CROs were identified as a valuable resource for delivering comprehensive drug discovery capabilities, and facilitating access to expertise and relatively small start-up costs for new companies by relieving the need to recruit in-house. There is a large diversity in CRO offerings from large CROs with multiple offerings across the drug discovery pathway, to increasingly specialised CROs which offer a focused skill set for certain aspects. Many are highly innovative and are becoming important partners in the drug discovery landscape, particularly as some organisations may move towards more 'virtual' drug discovery. However, it was noted that there may still be some negative perceptions of the CRO sector as lacking innovation and leadership, and so it is important to ensure

[19] Wellcome (2016). *Wellcome Trust Monitor Report Wave 3: Tracking public views on science and biomedical research* www.wellcome.ac.uk/sites/default/files/monitor-wave3-full-wellcome-apr16.pdf
[20] Academy of Medical Sciences (2016). *Perspectives on conflicts of interest.* www.acmedsci.ac.uk/download.php?f=file&i=34042

continued engagement with this sector and build an understanding of its offering to the UK drug discovery ecosystem.

The biotech sector in the UK is also a valuable contributor to drug discovery and delegates discussed the importance of both encouraging biotech start-ups (including spin-outs from pharmaceutical companies and academia) and growing existing biotech companies. It was suggested that a more entrepreneurial culture could be supported through increased numbers of small grants and mentoring schemes, industry placements, and support for generating new spin-off companies. In addition, there was consensus that biotechs should be supported to become sustainable and self-sufficient SMEs where possible to maintain the vibrant ecosystem within the UK; the suggested steps highlighted in the 'Funding models' section should support this.

The virtual company: innovation in discovery

Dr Mason described his involvement as head of the virtual company XO1 developing a novel anticoagulant, which was run virtually through outsourcing with only a single permanent employee.[21] He explained that the company was centred around a 'brains trust' of the founders and consultants used for core pipeline and design decisions who were incentivised for success through equity in the firm. All other work was outsourced across academic scientists and CROs for execution of preclinical models, manufacturing and regulatory work. Finance, IT and Intellectual Property was also all outsourced to appropriate experts. In addition, a global approach was coordinated to ensure access to the best skills and organisations irrespective of location. Dr Mason termed this a *'Hollywood model'* of working where the company functions in the same way as a Hollywood film production with a team of experts assembled solely for the specific project, and with the venture capitalist acting like a film studio, providing funding and general direction.

Dr Mason asserted that the virtual model enables a flexible, international and highly capital efficient approach to be taken to drug discovery that ensures access to the highest quality talent at reduced cost. Furthermore, when there are financial pressures associated with the unpredictability of early research and innovation, expenditure can be temporarily scaled back with relative ease to allow resources to be diverted to addressing problems.

Metrics and evaluation

There was widespread consensus that metrics are needed for the UK drug discovery landscape to evaluate different funding strategies, direct future areas of focus for funding, allow comparisons between the UK and the global ecosystem to attract investment, and identify areas for improvement. It was agreed that these metrics are particularly important for drug discovery as reflected in the ABPI report, as this is one of the most competitive elements of global R&D. However, due to concerns around privacy and IP, preclinical data can be more challenging to collect than at other stages of R&D. Important metrics that were suggested include start up and survival rates of biotech companies, return on VC investment and effectiveness of open innovation and collaborative models. It was suggested that organisations such as the BioIndustry Association (BIA), ABPI, or other trade bodies and research institutes could contribute these metrics but the fragmentation of the discovery landscape may make this difficult.

[21] http://www.xo1.co.uk/

Finally, it is important to create a positive environment for uptake and adoption of innovation in the NHS so that drug discovery science can be translated into clinical practice. It was suggested that industry can perceive the UK to be a relatively slow adopter of innovation compared with other healthcare systems, and so it is important to address any barriers to patient access to ensure that the UK is seen as a world-leading life sciences ecosystem.

Opportunities

- Clearer communication around expectations for drug discovery processes is needed between all sectors involved. This can be facilitated through collaborative frameworks and closer working across sectors as well as through consortia.
- Establishing common definitions and guidelines around standard practice for target identification and validation across sectors to reduce variation in practice and facilitate collaboration.
- The discovery environment will need to shift to focus more on impact of drug discovery activities rather than maintaining a narrow focus on income and publication.
- Better supporting uptake and adoption in the NHS to ensure upstream integration of new innovative technologies into the healthcare system.
- Better communication around the benefits of a diverse drug discovery ecosystem and in particular, highlighting the benefits of the vibrant CRO and biotech sectors.
- Continued collection of metrics on the drug discovery landscape. Bodies such as trade associations could scope metrics that can be realistically collected from members of the ecosystem and encourage the provision of these metrics.

Annex 1: Stakeholder presentations

ABPI survey of the drug discovery landscape

Mike Thompson, Chief Executive, The Association of the British Pharmaceutical Industry, recognised that the UK is in a period of significant discontinuity, bringing both opportunities and challenges. He emphasised the value of a clear Industrial Strategy in allowing the UK to continue to compete effectively at a global level and aligning sectors across the life sciences ecosystem. With decreasing in-house activity within industry and increasing outward investment, he stressed that building a sustainable ecosystem is ever more important with the reliance on such a broad range of stakeholders. Mr Thompson highlighted that discovery research is globally mobile and cautioned that industry investment in the UK is not keeping pace with global investment in drug discovery research. In addition, there is an overarching need to address patient access and uptake of new therapies in the NHS to pull through the innovation emerging from the excellent life sciences research base. Finally, he recognised the significant opportunities for the ecosystem in addressing these needs and capitalising on the unique offerings of the NHS.

Dr Rebecca Lumsden, Head of Science Policy, The Association of the British Pharmaceutical Industry, introduced the findings from the ABPI report, which provided an evidence base on the drug discovery landscape at the meeting.

Employment and investment

In the last 5-10 years there has been a significant shift in the approach to drug discovery from a closed in-house model to a more open and networked way of working. There has been a reduction in in-house drug discovery employment in the UK by large pharmaceutical companies. However, there has been an increase in in-house employment by many SMEs, CROs, and academic centres. Dr Lumsden noted that whilst there have been mixed patterns of in-house investment in discovery by large companies, the large majority have increased their collaborative and outsourced investment in the UK, reflecting changing models for drug discovery, and facilitating the dynamic growth of other components in the UK ecosystem. Additionally, there was a reported increase in number of UK-based staff co-ordinating global drug discovery activities from the UK, suggesting that the UK retains a global reach and influence in discovery.

Overall, the ABPI survey suggested that investment in drug discovery in the UK has mostly increased or been sustained in the last 5-10 years. However, importantly, this does not seem to be keeping pace with the increase in investment seen globally, so Dr Lumsden noted that proportionally the UK may be *'losing out'*; for example, 24% of companies reported a decrease in overall investment of drug discovery in the UK, compared with 9% reported globally.

Collaboration and outsourcing

Almost all biopharmaceutical companies have increased their collaboration in drug discovery, working with a broad range of partners including CROs, biotechs, catapults, academia and charities. Whilst the most common form of collaborations were still 1:1 commercial collaborations, pre-competitive models have become increasingly common. Collaborative work in the UK generally appears to focus on core target identification and validation amongst other areas, and Dr Lumsden felt that this was reflective of the strength of the UK academic research base. She explained that aspects of discovery such as toxicology and medicinal chemistry were often outsourced, and this trend in outsourcing has led to CROs becoming an increasingly important component of the drug discovery landscape both in the UK and globally over the past decade. This is supported by a reported increase in commissioning to CROs, and it was recognised that there is a growing specialist CRO base in the UK. Notably, she identified potential gaps in the UK for capabilities such as High Throughput Screening (HTS), which is most often conducted abroad.

Overall, Dr Lumsden noted the benefits of an increasingly collaborative approach in research, but noted that some areas are still predominantly initiated outside of the UK such as HTS. Whilst these could be considered a weakness, Dr Lumsden challenged participants to consider whether the UK should develop all drug discovery capabilities or if, recognising the global nature of drug discovery, it should focus on building strengths in specific areas. Despite the UK's collaborative strength, Dr Lumsden emphasised that there is a need to continue to develop the drug discovery environment to ensure that we do not continue to fall behind global investment in drug discovery.

The evolution of the drug discovery landscape

Emerging trends in drug discovery

Dr Richard Mason, Head of Johnson & Johnson Innovation, began by emphasising the changing *'nature of the firm'* - an economic concept from the 1930s which reasons that in-house company activity exists as the most cost-effective method by which to organise and conduct business.[22] More recently, it has become increasingly efficient to organise business through the marketplace, and this has been followed by growing innovative models for drug discovery and a move away from in-house employment as evidenced by the ABPI report.

Dr Mason noted that the rate of innovation has remained generally stable in research and development (R&D) but there has been a decline in productivity with the efficiency of R&D indeed halving every nine years.[23] The reasons behind this are multifactorial and he noted two particular challenges highlighted by Jack Scannell *et al* that may have contributed to this decline. Firstly, it has become increasingly challenging to develop new medicines where effective medicines are now available for many conditions, and so new medicines must not just treat the disease but demonstrate significant value over existing interventions. Secondly, a *'brute force bias'* approach has been adopted where companies have merged and expanded, and have thrown increasing finance and resource at R&D, but the size of such organisations can bring diseconomies of scale including lack of agility and innovative capacity. Dr Mason argued that this increase in the size of companies has not increased the predictability of biomedical innovation or where it occurs (i.e. *inside* the boundaries of the firm), and so companies are increasingly seeking to find and access innovation wherever it is taking place in the world, *outside* the boundaries of the firm.

The future of innovation in drug discovery

Dr Mason shared his positive outlook on the UK drug discovery environment and emphasised the need for the sector to consider new ways to access and accelerate innovation. Virtual companies provide one such framework where a company can be built entirely around outsourced talent. Another example of this is using innovation centres to coordinate drug discovery activities with multiple external parties, and enabling access to a wider stakeholder base. Johnson & Johnson have also used this model for JLABS in the USA which function as incubators for biopharmaceutical innovation through siting many different companies – these match the needs of the ecosystem and have the ability to be agile with quick assembly and disassembly to enable organisation around innovation. Dr Mason felt that such different models for drug discovery enable industry, and other key sectors, to be broad-minded around the measures for success.

The role of Contract Research Organisations

Dr Thomas Mander, Chief Operating Officer, Domainex, described the thriving CRO sector in the UK comprising both specialist and non-specialist firms. He explained that this growing sector employs significant numbers of life scientists

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[22] Coase RH. (1937). *The Nature of the Firm.* Economica **4(16)**, 386-405.
[23] Scannell J, *et al.* (2012). *Diagnosing the decline in pharmaceutical R&D efficiency.* Nature Reviews Drug Discovery **11**, 191-200.

and is vital to the UK's drug discovery ecosystem, often acting as great innovators as well as service providers. Interestingly, he noted that despite the establishment of substantial providers in Europe, Asia and other areas, the USA does not contribute substantially to this sector in contrast to other parts of the discovery landscape.

Growth in outsourcing of drug discovery

In general, CROs have benefitted from downsizing of in-house activity in large pharmaceutical companies and the concomitant rise in outsourcing. In addition, Dr Mander discussed how CROs are becoming vital contributors to the drug discovery landscape, and are themselves moving towards greater collaboration and open approaches to innovation. He noted, in particular, the value of increasing interaction with academia both as a vital client base and source of partnerships and expertise. He also highlighted the extensive opportunity presented by the UK's strengths in drug discovery, providing a strong science base and access to talent. Alongside these growing interactions and partnerships, CROs have benefitted from expanded investment through UK Government initiatives such as R&D tax credits and the Patent Box, as well as using EU schemes such as Horizon 2020 which are critical for facilitating international business and collaboration.

Challenges for service providers

However, Dr Mander emphasised that there are challenges in this environment that need to be overcome. These include the potential impact of Brexit on the UK's access to EU-funded programmes and talent and skills, and a need to mitigate the impact of post-referendum uncertainty for smaller companies. In addition, Dr Mander observed that the CRO sector is fragmented and competitive with substantial providers across the world, and so UK CROs will need to offer the highest-quality differentiated services to continue to position themselves as world leaders.

UK biotechs in drug discovery

Dr Fiona Marshall FMedSci, Chief Scientific Officer, Heptares Therapeutics, described the vibrant biotech ecosystem in the UK, formed of spin-out companies from academia as well as pharmaceutical companies. She emphasised the increasing reliance on biotechs to support company pipelines, facilitate access to new technologies and increase working efficiencies, as well as acting as an essential component of collaborative partnerships.

Outsourcing from biotechs

Dr Marshall explained that most UK biotechs outsource to some extent through CROs and that this trend is increasing, echoing trends towards more 'virtual companies' as described by Dr Mason, and reflecting the increasing importance of CROs in the landscape. Commonly outsourced functions include areas such as synthetic and medicinal chemistry; routine tasks such as HTS; ADME (absorption, distribution, metabolism, and elimination) and DMPK (drug metabolism and pharmacokinetics); and *in-vivo* studies. Typically, most biology is outsourced within the UK and Dr Marshall noted the importance of criteria such as quality, control, throughput, cost, and turnaround time in decisions about outsourcing in the UK or globally, as well as limitations on which companies can be used through grant requirements. She emphasised that the UK particularly excels in quality and control, and competes successfully in the global market, but differences in research frameworks and training between countries can make them more attractive for specific tasks. Turnaround can also be faster in other countries.

Collaboration and funding

Biotechs are actively involved in cross-sector collaborations with charities, academia and large pharmaceutical companies both in the UK and abroad. Dr Marshall described extensive collaboration with large pharmaceutical companies involving technology transfer, licensing, and collaborative working, highlighting the important role that biotechs play in bringing both funding, and occasionally employment, to the UK from global companies. Collaborations with academia are also vital for facilitating access to the UK's first class research base. For example, these partnerships are often used for novel target identification and validation and translation of science, such as those with the Sheffield

Institute for Translational Neuroscience (SiTRAN).[24] Dr Marshall observed that currently, most biotech collaborations are 1:1 and expressed support for more collaboration involving multiple groups. Better collaboration between biotechs would have advantages for risk sharing. Access to major infrastructure and equipment, such as the Diamond Light Source science facility in Oxfordshire, is one important mechanism for supporting such collaboration.

Dr Marshall emphasised that grant funding is critical for the biotech industry, particularly for smaller start-ups, and highlighted the opportunity for UK biotechs to access funding from outside of the UK as demonstrated by the partnership between Heptares and the US National Institute of Drug Abuse (National Institutes of Health). Grants provided by charities such as the Wellcome Seeding Drug Discovery programme are increasingly important in sustaining biotech projects and EU grants have also been vital for international and multidisciplinary research.

Future opportunities for drug discovery

Overall, Dr Marshall reiterated the increasing role of biotechs in the UK drug discovery landscape and the opportunity to build on the successes of collaborative research across sectors and increased outsourcing to CROs. She noted that whilst the UK biotech industry has grown in recent years, it is not growing as rapidly as CROs. This may be due to the current gap in drug discovery skills which biotechs depend upon, such as bioinformaticians, biophysics, and DMPK experts, and there is a need to ensure sustainability of the future skills pipeline given the decrease of in-house training of scientists by large pharmaceutical companies. In addition, she felt that new ways to build biotech skills and capabilities should be explored and described the opportunities of licensing deals at earlier stages of drug discovery and retaining drug candidates further into the development process.

The academic perspective of drug discovery

Cancer drug discovery in UK

Professor Paul Workman FRS FMedSci, Chief Executive and President, Institute of Cancer Research (ICR), began by highlighting that drug discovery in cancer has been a highly active and innovative area of research, with survival rates doubling since the 1970s. In recent years, the UK has championed a shift from broad spectrum cytotoxic therapies towards personalised targeted therapies in cancer drug discovery and many precision medicines have now been approved alongside predictive biomarkers. However, despite this progress, Professor Workman expressed concern about the overall low survival rates for cancer patients in the UK, particularly for certain types of cancer.

To build on current progress, Professor Workman argued that the druggable cancer genome should be extended to ensure that there are drugs identified for all key molecular pathways. With the increasing challenge of drug resistance, he emphasised that ways to target cancer evolution, adaptation and tumour heterogeneity must be prioritised such as through exploring opportunities for combination therapy and immunotherapy. Finally, he noted that pricing of treatments in oncology can be challenging, and the need for greater robustness in target validation plus the requirement for more predictive *in-vivo* models. It was argued that addressing these priorities will require involvement of the whole research ecosystem.

Professional drug discovery in a not-for-profit setting

Professor Workman stressed that academia and not-for-profit organisations can play a critical role in bridging the valley of death in this area to drive sustainable innovation. He asserted that this helps to overcome challenges such as a risk-averse commercial environment; downsizing of large pharmaceutical companies; pricing issues and constraints; and relative lack of long term capital investment in UK biotech compared with other leading areas for drug discovery such as Boston. Therefore he suggested that models similar to that adopted at the ICR of professional drug discovery

[24] www.sitran.org/

in an academic, not-for-profit setting, offer the opportunity to overcome the above challenges, potentially saving resource and de-risking targets for industry.

The ICR operates to industry standards and scale and furthers its capabilities through CRO outsourcing and industry collaboration where required, and there are multiple examples of drugs that have been developed through this model. In addition to academic expertise in basic cancer research, direct access to the Royal Marsden Hospital supports clinical input at every stage of drug discovery and this collaboration has also allowed clinical trials to be effectively carried out in-house. Recruiting senior researchers with industry training in areas such as medicinal chemistry, drug discovery biology and project leadership was critical for success and Professor Workman felt that such centres also provide exciting opportunities for training both in scientific methodology and crucial soft skills such as managing relationships and partnerships.

Expanding the ICR model

Professor Workman argued that professional high quality drug discovery in the context of a non-profit institution has the potential to make a significant contribution to the drug discovery landscape. However, he emphasised that establishing the correct culture as well as skills base in these centres is fundamental for professional drug discovery. An industry-style focus on standards and results should be integrated alongside exploratory and *'curiosity-driven'* research, and basic and clinical researchers working alongside entrepreneurial, industry-trained staff has been essential. Further to this, research institutes offer the opportunity for a paradigm shift away from short-term micromanaged budgets towards long term support for a portfolio of projects with associated flexibility. For example, ICR currently maintains a portfolio of drug development projects in addition to exploratory and early stage work, which provides the flexibility to focus financial support on the most promising drug discovery projects at the most opportune times, enabling risk-taking and development of a high-quality, cost-effective and unbiased pipeline.

Drug discovery and the patient

Drug discovery in dementia

Moving to focus on Alzheimer's disease, Dr David Reynolds, Chief Scientific Officer, Alzheimer's Research UK, observed that the drug discovery landscape can vary greatly between disease areas and a more tailored research approach offers significant potential to improve treatments in dementia. He noted a number of unique obstacles to dementia drug discovery including current clinical trial endpoints which lack sensitivity and specificity. Therefore new biomarkers for effectiveness would be hugely beneficial and Dr Reynolds emphasised the need to start developing these biomarkers alongside early drug discovery processes. Dementia is one of the few major diseases for which there are no treatments that modify the disease progression and he noted that solving this problem had been the major focus of industry efforts for the last twenty years or more. He acknowledged that this focus was important, but also highlighted that symptomatic treatments for both cognitive deficits and the other behavioural issues associated with dementia should not be neglected as this is also an area of high unmet patient need.

As described earlier, targeted investment in drug discovery for diseases such as cancer over recent years has yielded exciting developments in the field. Dr Reynolds felt that similar levels of investment in Alzheimer's would also offer tangible benefits whereas in reality, the number of companies working in this area has decreased over the past decade due to the slow progress in drug discovery and with, thus far, no products approved. Therefore alternative models and sources of investment have offered exciting potential to bolster progress. This includes the Dementia Discovery Fund, a consortium between industry, charity and Government, and the NeuroMap consortium between the Medical Research Council and charities, as well as the Drug Discovery Alliance and Dementia Consortium established by

Alzheimer's Research UK.[25,26,27] Dr Reynolds emphasised that industry maintains an interest in the field due to its large market size and so current initiatives aim to bridge the translational gap between scientific understanding, high profile papers suggesting new targets, and target validation sufficient to attract industry to start drug discovery programmes.

Involving patients in drug discovery and development

Alzheimer's Research UK is working to involve patients in every aspect of drug discovery and development, both raising awareness of the R&D process and ensuring that it is shaped through patient input. Involving patients in research can be difficult due to lack of awareness about research opportunities as well as due to the nature of dementia symptoms which can cause complications in aspects such as consent and logistical requirements of participation. Therefore Dr Reynolds noted that dementia research has yet been fully driven by patient involvement and the 'Join Dementia Research' (JDR) initiative aims to resolve these issues, acting as a leading public registry to draw together large numbers of potential patients for trials.[28] Researchers are able to use the JDR system to identify patients to invite to participate in studies but it has also proved an important tool for facilitating patient involvement in earlier stages of dementia drug discovery. Patients and carers can provide insight into feasibility of trials through the JDR and Alzheimer's Research UK has used this information to include a lay person review in all grant applications. In this manner, Dr Reynolds considered the JDR an excellent resource for patient outreach to improve the rate and costs of drug discovery and enhance dementia research as a whole.

[25] www.theddfund.com/

[26] www.medicinesaccelerationprogram.org/

[27] www.alzheimersresearchuk.org/for-researchers/research-opportunities/centres-and-institutes/

[28] www.joindementiaresearch.nihr.ac.uk/

Annex 2: Participant List

Chairs and speakers

Professor Herbie Newell FMedSci (co-chair), Emeritus Professor of Cancer Therapeutics, Newcastle University
Dr Neil Weir (co-chair), Senior Vice President of Discovery, UCB
Dr Harren Jhoti FMedSci, President and CEO, Astex
Professor Sir Robert Lechler PMedSci, President, Academy of Medical Sciences
Dr Rebecca Lumsden, Head of Science Policy, Association of the British Pharmaceutical Industry
Dr Tom Mander, Chief Operating Officer, Domainex
Dr Fiona Marshall FMedSci, Chief Scientific Officer, Heptares Therapeutics
Dr Richard Mason, Head of Johnson & Johnson Innovation, Johnson & Johnson
Dr David Reynolds, Chief Scientific Officer, Alzheimer's Research UK
Dr David Roblin, Chief Operating Officer and Director of Translation, The Francis Crick Institute
Professor Malcolm Skingle, Director – Academic Liaison, GlaxoSmithKline
Mr Mike Thompson, Chief Executive Officer, Association of the British Pharmaceutical Industry
Professor Paul Workman FRS FMedSci, Chief Executive and President, Institute of Cancer Research

Participants

Dr Alex Amey, Associate Head of Business Interaction – Health & Biorenewables, Biotechnology and Biological Sciences Research Council
Professor Richard Barker OBE, Director, CASMI
Professor Chas Bountra, Head of Structural Genomics Consortium, University of Oxford
Dr Julie Brady, Business Development Manager for Drug Discovery, University of Dundee
Dr Justin Bryans, Director of Drug Discovery, MRC Technology
Dr Ian Campbell, Director of the Research School of Design, Innovate UK
Dr Kathryn Chapman, Executive Manager, Milner Therapeutics Consortium, University of Cambridge
Dr Nick Clarke, Project Leader, Pfizer
Dr Trafford Clarke, Managing Director, Lilly Research Centre, Lilly
Professor John Collinge CBE FRS FMedSci, Head, Department of Neurodegenerative Disease, University College London
Mr Lee Coney, Chief Scientific Officer - Biologics & Corporate Vice President, Envigo
Mr David Cronk, Director, Hit Discovery, Charles River Laboratories
Dr Suzanne Dilly, Chief Scientific Officer, ValiRx
Dr Philip Driver, Senior Programme Manager, Royal Society of Chemistry
Professor Martin Drysdale, Head of Drug Discovery Programme, Beatson Institute for Cancer Research
Dr David Griffiths-Johnson, Head of Innovation, Office for Life Sciences
Dr Peter Hamley, Global Head – External Innovation and Sourcing, Drug Discovery Platform, Sanofi
Dr John Harris, Chief Executive Officer, OBN
Dr Louise Jones, Head of Translation Research, Medical Research Council
Dr Philip Jones, Director, European Screening Centre, University of Dundee
Professor John Ladbury, Dean Faculty of Biological Sciences and Professor of Mechanistic Biology, University of Leeds
Mr Andrew McConaghie, Managing Editor, Pharmaphorum
Dr Stephen Megit, Associate Director of Business Development, Immunocore
Mr Chris Molloy, Chief Executive, Medicines Discovery Catapult
Dr Declan Mulkeen, Chief Science Officer, Medical Research Council
Dr Peter Newham, Global Head Discovery Safety, Drug Safety & Metabolism, AstraZeneca
Dr Sally Nicholas, Business Analyst, Wellcome Trust
Dr Terry O'Neill, Head of Health, Knowledge Transfer Network
Dr Liz Philpots, Head of Research & Impact, Association of Medical Research Charities
Professor Christopher Pugh FMedSci, Professor of Renal Medicine, University of Oxford
Professor Stephen Rennard, Chief Clinical Scientist, Clinical Discovery Unit, AstraZeneca
Dr Richard Seabrook, Head of Business Development Innovations, Wellcome Trust

Dame Pamela Shaw DBE FMedSci, Director of the Sheffield Institute for Translational Neuroscience (SITraN), University of Sheffield
Dr James Staddon, Director of Open Innovation, Eisai
Professor Simon Ward, Director, Sussex Drug Discovery Centre, University of Sussex
Professor Paul Whiting, Chief Scientific Officer, UCL Drug Discovery Institute, University College London
Dr Rob Williams, Chief Drug Development Scientist, Cancer Research UK
Dr Louise Wood, Director of Research Infrastructure and Growth, Department of Health
Professor Paul Wyatt FRSE, Head of the Drug Discovery Unit, University of Dundee
Dr Anna Zecharia, Head of Education and Training, British Pharmacological Society

Secretariat
Ms Liberty Dixon, Policy Officer, Academy of Medical Sciences
Ms Katharine Fox, Policy Intern, Academy of Medical Sciences
Dr Mehwaesh Islam, Policy Officer, Academy of Medical Sciences
Dr Nicola Platt, Science Policy Officer, Association of the British Pharmaceutical Industry
Dr Rachel Quinn, Director, Medical Science Policy, Academy of Medical Sciences
Mr Andrew Ross, Media Relations Manager, Association of the British Pharmaceutical Industry
Mr Robert Smith, Social Media Content Editor, Association of the British Pharmaceutical Industry

Annex 3: Agenda

09.30-10.15	**Registration**
10.15-10.35	**Welcome** Professor Herbie Newell FMedSci (co-chair), Emeritus Professor of Cancer Therapeutics, Newcastle University
The current UK environment for preclinical drug discovery Professor Herbie Newell FMedSci (co-chair), Emeritus Professor of Cancer Therapeutics, Newcastle University	
10.35-10.55	**Introduction to the ABPI survey** Mike Thompson, Chief Executive Officer, ABPI and Dr Rebecca Lumsden, Head of Science Policy, ABPI
10.55-11.10	**The evolution of the UK drug discovery landscape** Dr Richard Mason, Head of Johnson & Johnson Innovation, Johnson & Johnson
11.10-11.25	**The role of Contract Research Organisations** Dr Thomas Mander, Chief Operating Officer, Domainex
11.25-11.50	**Tea and coffee**
11.50-12.05	**UK biotechs in drug discovery** Dr Fiona Marshall FMedSci, Chief Science Officer, Heptares Therapeutics
12.05-12.20	**The academic perspective of drug discovery** Professor Paul Workman FRS FMedSci, Chief Executive and President, Institute of Cancer Research
12.20-12.35	**Drug discovery and the patient** Dr David Reynolds, Chief Scientific Officer, Alzheimer's Research UK
12.35-13.15	**Panel discussion: where do we go from here?** With all speakers
13.15-14.00	**Lunch**
How can we use this information to develop and refine UK drug discovery? Dr Neil Weir (co-chair), Senior Vice President of Discovery, UCB	
14.00-14.10	**Introduction to the workshop sessions** Dr Neil Weir (co-chair), Senior Vice President of Discovery, UCB
14.10-15.10	**Break-out sessions** 1. Changing drug discovery science. How can the UK be world leading in drug discovery science in 10-15 years? Chair: Dr Harren Jhoti, President and CEO, Astex Pharmaceuticals 2. A changing workforce. How can the UK build capacity and capability to maintain its leading role in drug discovery? Chair: Dr Malcolm Skingle, Director – Academic Liaison, GlaxoSmithKline 3. A changing landscape. How can the UK landscape be built to facilitate increased collaboration, open innovation, and growth? Chair: Dr David Roblin, Chief Operating Officer, The Crick Institute
15.10-15.40	**Tea and coffee**
15.40-16.10	**Break-out sessions cont'd**
16.10-16.50	**Feedback and discussion** Each group to feed back findings, for discussion with all participants.
16.50-17.00	**Conclusions and next steps** Dr Neil Weir (co-chair), Senior Vice President of Discovery, UCB
17.00	**Drinks reception**

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