

The healthcare industry's evolving role in translational research

an opportunity for competitive advantage

During the 20th century, medical research has observed enormous advances in basic science discovery, highlighted by the sequencing of the human genome. However, we have not witnessed a corresponding success in the widespread application of these advances into medical practice; bridging the gap between the discoveries achieved at the 'bench' and interventions and therapies at the 'bedside' remain a challenge. This gap has been singled out as having an unwelcome effect not only on patient care but, more broadly, on a country's economic development. In fact, more than 40 years ago, British economists Charles Carter and Bruce Williams noted that "it is easy to impede [economic] growth by excessive research, by having too high a percentage of scientific manpower engaged in adding to the stock of knowledge and too small a percentage engaged in using it."

The on-going challenge for the industry to deliver on clinical application highlights the persistence of a drug development model that has not adapted to changes in science, public perception of the pharmaceutical industry, or the marketplace. Until now, high profit margins have shielded drug development from the kind of pressures that would prompt reform. The spate of mergers in the past decade among many of the largest drug companies has exacerbated the problem by adding the complexity that mergers bring to an already inefficient and outmoded process. As a result, the industry has not given the translational or 'bench to bedside' aspect of the pipeline the full attention deserved.

As part of recent work Arthur D. Little completed on the topic of translational research, we inter-

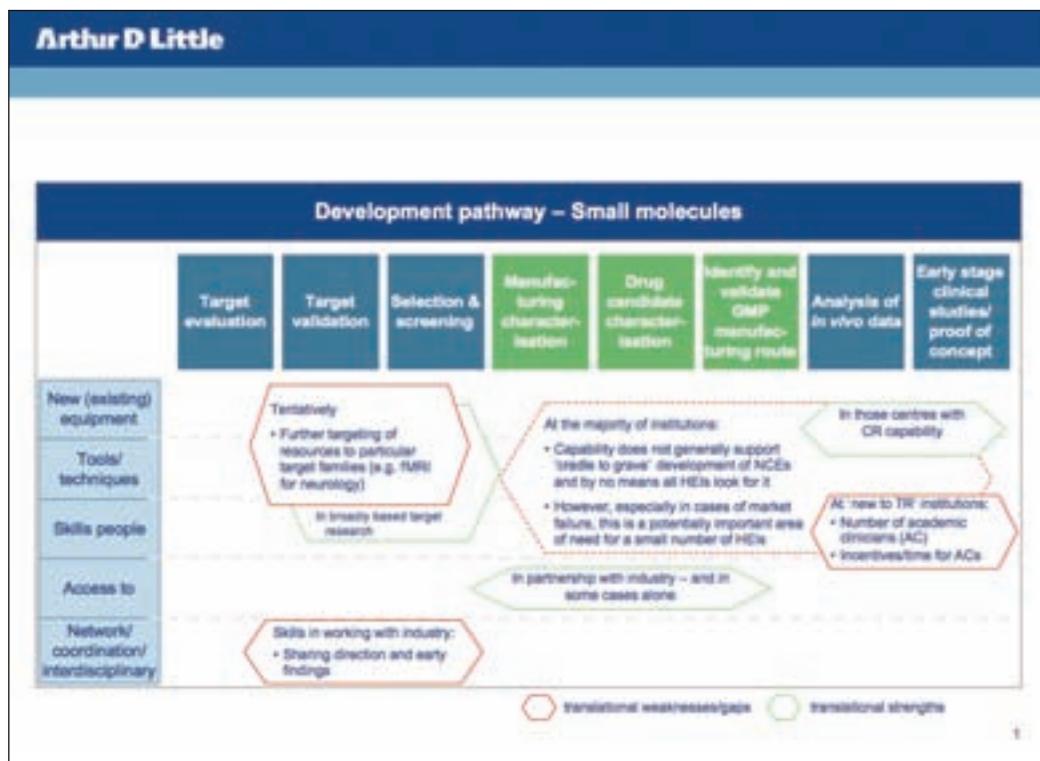
viewed a number of researchers within academia and industry who spoke openly about the challenges in translation. We also spoke to institutional administrators, charities and public funding organisations. They provided us with many insights into the current state of translational research in Europe and the US, including what academia and industry should do in order to achieve better, faster translational results, to the benefit of both patients and themselves.

What is translational research?

'Translation' refers to the application of the results of basic biomedical research to the practice of medicine. More specifically, it describes the process of converting discoveries made in the laboratory into clinical interventions that provide a direct benefit

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to human health. Laboratory discoveries are not typically made in a form ready for adoption by the clinician to treat patients; therefore, research doesn't end with the discovery in the laboratory. In fact, this constitutes the start on the development pathway leading to the creation of a treatment suitable for humans.

The translational process has generally been viewed as a complex and protracted one, lacking clearly defined start and end points. Historically, it was represented by a single step on a linear path between scientific discovery and its clinical application (often a very big step – the translational step that resulted in penicillin took nearly 20 years). Today, however, it is no longer linear or unidirectional. Translation can now occur from bench to bedside and bedside to bench, often with many journeys in both directions. Therefore, we have adopted the following descriptor for translational research: Research which facilitates or enables the more rapid or more effective transition of basic research towards large scale evaluation (to validate use for humans).

The process of new drug discovery and their full evaluation in patients incorporates five fundamental extrapolations:

- 1 From physiochemical properties to biology.
- 2 From *in vitro* to *in vivo* (within animals and within humans).

- 3 From animals to healthy human volunteers, referred to as Phase I human safety and pharmacological proof of concept.
- 4 From single doses to multiple doses.
- 5 From healthy volunteers to patients.

The extrapolation from animals to humans is generally viewed as the most significant and is at the centre of translational research. However, broadly speaking, translational research encompasses all steps listed above, with the exception of the first.

An intriguing aspect of translational research is that it sits squarely between academia and industry. This is a consequence of the aim of researchers on both sides to deliver efficacious interventions and therapies to benefit human health.

Industry's approach

Over the years, industry collaboration with academia has figured prominently in numerous translational successes, including angioplasty, recombinant growth hormone, stenting for coronary artery disease, and many new drug treatments and medical devices. However, the drug discovery and development process as pursued by the biotechnology and pharmaceutical industries has come under criticism. The main objections have focused on the time required to develop products fit for human

use, inefficiencies in the process and expense. Current conventional wisdom states that up to 15 years are required to take an original idea to product launch, that about one billion US dollars will be invested, and that only one in every 5,000 to 10,000 compounds synthesised will actually become a commercial product. It has been proposed, however, that seven years is a reasonable target timeframe and a success rate of 1 in 250 compounds is feasible. Attacking these challenges forms a core objective of translational medicine.

Since it has been largely accepted that there will be no more major medical research breakthroughs (certainly not a sufficient number of consistent and sizeable discoveries to support a business model) and the noteworthy mergers have already taken place, Pharma has known for some time that it must re-evaluate its approach to the developmental pathway. Furthermore, Pharma has always had its limitations. These include a lack of access to patients; dissension at many levels between discovery and development; the increasing physical atomisation of the enterprise; and an inflexibility and inertia derived from a previously profitable way of doing business.

Additional pressures on the traditional business model include a growing pressure on global pricing and the advent of both China and India as competitors in new drug development. Accepting the fact that the blockbuster drug discoveries are a thing of the past and that the traditional business model is under threat both internally and externally increases the pressure for Pharma to re-evaluate its position on translation.

The evolution of the bio-technology industry has also impacted the incumbent model for medical research. The major players in the pharmaceutical industry responded to this alternative approach to expand their presence along the developmental pathway while maintaining the ability to carefully manage investment levels and risk. However, all stakeholders in medical research have realised that the gap in translation previously filled by smaller bio-technology firms continues to exist. This is because bio-tech SMEs have been less successful than expected in translating advances in basic science into therapies. In addition, investment from the financial sector to support bio-tech SMEs has recently become much scarcer, reopening the gap in translation that had only just begun to close.

Successful collaboration with academia continues to be the promising opportunity for Pharma. By identifying the optimal approach that capitalises on the strengths of each party and by solving the most common deficiencies that have appeared in

past collaborations, Pharma can establish a new model for translation, one focused on delivering a greater number of products and approaches versus a limited number of breakthroughs.

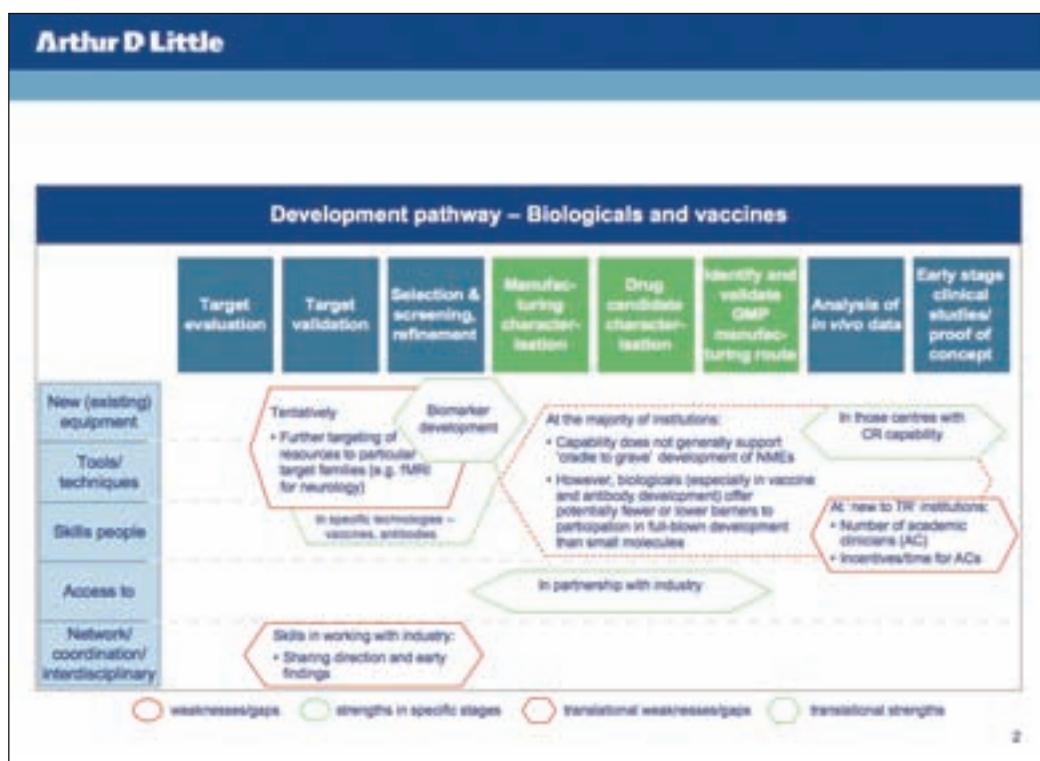
Academia and industry

From the perspective of the pharmaceutical industry, the universities have become a familiar component in the early stages of research, identifying and characterising biological targets. Pharmaceutical companies have been divesting from early stage drug discovery activities, and the resulting gap is being filled by the universities, and, as mentioned earlier, (a shrinking pool of) bio-technology companies. However, some universities recognise that there are opportunities for still deeper industrial collaborations, with greater sharing of research goals and direction. Some of the best collaborations are found not in the 'core' of the traditional pathway, such as drug discovery, but in supporting and enabling activities, in areas such as bio-marker identification and development, and imaging science.

Academics often welcome the direction industry is able to provide to their research. Industry, in return, seeks access to patient populations (for example in their relationships with the new academic health science centres), specific research expertise they do not hold in-house, and broader access to the university's knowledge base. Funding remains an ingredient, but not a driver, of these relationships. Increasingly, the industrial domain of drug discovery is being pursued by academics on the basis of a set of three rationales:

- 1** Meeting areas of unmet need where discoveries would not necessarily be commercially appealing. The potential market may be small or impoverished, or the pharmaceutical company may have other products fulfilling the same niche, yet the social good of such treatments can be significant.
- 2** Having access to early directions and outputs in basic science and the opportunity to maintain a dialogue with researchers, contact with the development process, and access to the clinical outcomes uniquely places academia to translate discoveries more effectively, and innovate upon the development process.
- 3** Translating projects further down the development pathway allows the university to stake a greater claim to any commercial benefits arising from a product. They are also, however, absorbing more of the risk associated with development, especially in the current economic climate where early-stage venture capital funding is increasingly limited.

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Declining productivity combined with increasing costs within the pharmaceutical sector is driving the evolution of a new collaborative model where academia and industry identify and validate novel targets and define leads and candidates at the front end of the drug discovery pathway, while the pharmaceutical industry fulfils the role of an efficient development machine. Fundamental to this approach is a genuinely collaborative environment where academic contributions to translational research are rewarded with appropriately-structured funding, intellectual property ownership, and a share in future royalties.

One example that may prove to be a model for the future is the Drug Discovery and Development Centre (DDC) in Germany. With the help of the pharmaceutical industry, the Max Planck Institute and Max Planck Innovation set up the DDC, an incubator in two parts: the Lead Discovery Centre and the Development Company.

The Lead Discovery Centre focuses on taking hits along the development pathway to the point of a well-proven lead. Because the Max Planck Institute is itself only allowed under German law to perform basic research activities, the Lead Discovery Centre fulfils the translational gap by moving basic science to a more developed point, one more interesting commercially. The second part of the incubator, tentatively named the

Development Company and scheduled to launch by the end of 2009, will take a lead and develop it to the point of Phase II clinical trials. The Development Company is intended to be a technology transfer entity with responsibility for managing the licensing of results to an established firm, engineering the spin-out as a stand-alone enterprise, or providing co-investment of a viable project result.

What the Lead Discovery Centre and Development Company do is address the gap in translation identified in 2001. At that time, higher education institutions (HEIs) were only capable of providing basic science research; the number of bio-technology firms that could take leads forward had dwindled, and venture capital funding had dried up, widening a translation gap that had begun to narrow. What is more, the DDC bridges the gap created by a lack of networks among stakeholders, which had ensured that no other solution to the translational gap would be found.

While infrastructure sharing for translation can be actively encouraged, it may also prove beneficial (especially for the less commercially viable disease areas) to place resources like the DDC partly outside of the usual HEI structures. The DDC presents a good basis for the pharmaceutical sector and HEIs to establish together a similar 'neutral' forum for the development of collaborations focused on translation.

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Opportunities for industry

Academia's transforming outlook toward its role in translational research represents one of the most promising areas of opportunity for industry. Until now, the relationship between academia and industry has been clouded by the fact that industry tended to take the lion's share of profits by investing in later-stage research. One example of this has been to buy IP outright and develop it for human (commercial) applicability.

What has begun to change is academia's view toward the IP it develops alone. Increasingly, the universities strive to maintain control of their IP for as far along the development pathway as possible (that is, as long as grant money is available to finance it). If a university is able to carry forward a project as far as pre-clinical trials, the value of the IP is significantly enhanced, and their bargaining position with industry equally so. The result is a stake in the commercial outcome of the research. Academia and industry participate more as equals with both sharing in the outcome. This degree of competitiveness between academia bringing IP further forward to enhance its bargaining power and industry seeking to balance investment and risk will be a principal driver in shaping the future relationship between the two parties.

The increasing demand to be commercially astute will also steer universities toward more effective project management. It will also influence how departments structure themselves and utilise infrastructure, replacing the traditional attitude to staffing and securing resources with a more value-based approach. This will have a direct effect on the way in which HEIs seek funding. Where, in the past, a principal investigator would apply for a grant meant to pay for researchers and equipment, the trend now is to maintain a streamlined staff of project managers and to outsource skills or seek access to equipment not directly available to the project's staff.

Greater focus on effective project management and financing offers the possibility of ensuring more attention is given to building the research capabilities and skills necessary for candidate development further down the pathway. This will go a long way towards improving the bargaining power of universities, who will seek in future more commercially balanced partnerships with industry. And there are examples where industry has recognised this, particularly the early example of the Translational Medicine Research Collaboration run jointly by Wyeth and a consortium of Scottish universities and NHS trusts.

Although academia is proving itself to be capa-

ble of moving further into the translational aspects of the development path, industry and academia will need each other to successfully bridge the gap. The opportunity for industry is to recognise and pursue the possibility of establishing a new 'front-end' to the early discovery phase of drug development where, by working closely with academia, new therapeutic entities can be developed and taken to market. The most nimble and aggressive players in the industry can achieve competitive advantage by developing the collaborative business model that establishes that 'front-end.'

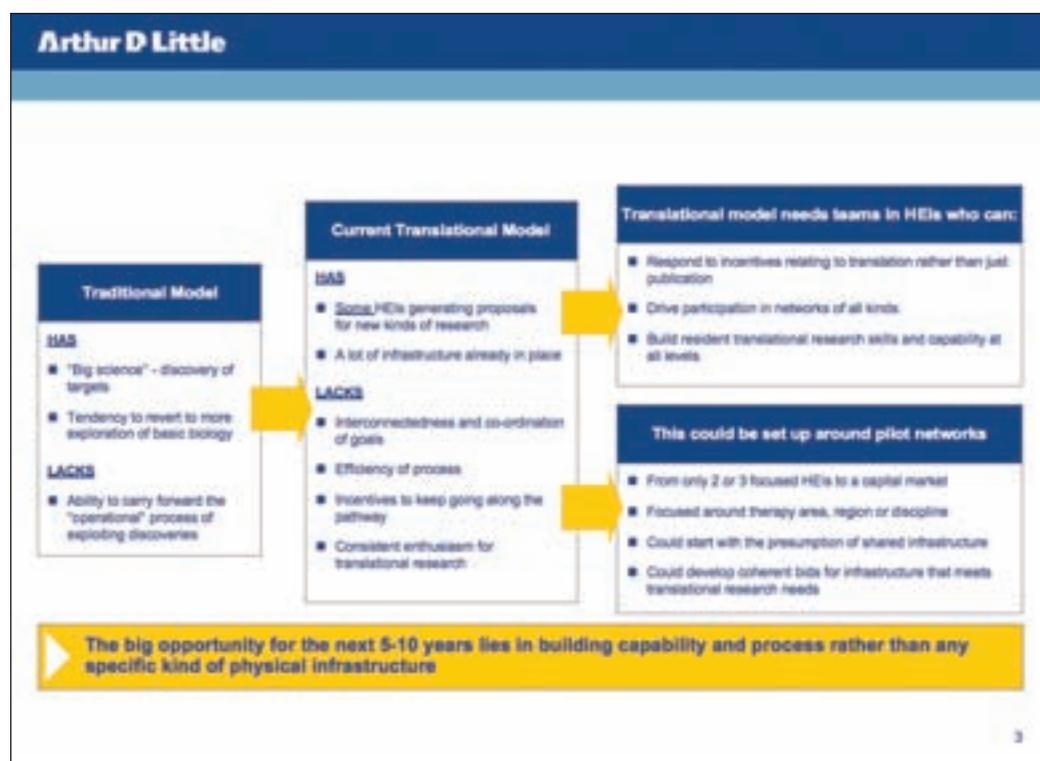
That model would need to address the challenges and weaknesses that have existed until now in past partnerships between academia and industry. The best business model would take into account the necessity for strict, industry-level project management capability within academia, implementation of standard operating guidelines and procedures, development of robust assay systems, and the provision for data reporting and control at the highest standard. Industry, for its part, must allow academia the freedom to pursue innovative research without applying their normal control mechanisms too rigidly. Importantly, the model must stipulate how all participants in the research will be rewarded for effort and success. Such a model could assume many forms – the Pharma industry, known for its innovation leadership, could, for example, lead the development of a capital market for discoveries and inventions, ensuring that the best projects would be translated by the most appropriate manufacturers.

Conclusion

Advantage may be achieved for those within industry which define the business model most appropriate for collaboration with academia. Late-stage entry into the development process and investment into proven science are no longer valid alternatives for the large biotechnology and pharmaceutical companies. Instead, they have the opportunity now to identify the level of risk that is appropriate to assume in development and define the approach to collaboration that rewards both parties fairly. Industry is in the position now to take the lead on providing two key aspects that would positively impact academic and industry collaboration: matchmaking and project management.

Matchmaking refers to the critical moment of project birth. A number of those we interviewed stressed that collaborations that are forced can rarely be successful. The most valuable projects have been those where researchers from different areas came together 'naturally', where the theme of

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the work proposed drove sufficient interest among the parties to not only motivate collaboration, but also to drive the project work forward after launch.

Project management comprises a whole collection of methods and techniques designed to ensure that developmental stages progress expeditiously and avoid problems, duplication and conflict. It requires a project manager who is not only capable in delivering the science but who is also able to manage all other aspects of a research project completed as collaboration among two or more parties.

Good project management brings order to complex and numerous tasks, such as providing work breakdown structures, managing external relationships, making project progression decisions, and keeping the overall work on track (to ensure timely publication for the academic contingent and hitting the milestones for the industry side). Project managers provide the tools to accurately capture data and information acquired during the course of the work, organise the necessary meetings among team members and stakeholders, maintain all records, and organise relevant team training. All of these activities are essential when working with a team of people from different disciplines and cultures who may have very specific backgrounds and skills and who do not otherwise work in tight project team environments. This type of approach to project management in medical research generally is quite

foreign to most academic researchers, but it is essential for translational research to be successful.

As the discipline of translational medicine evolves and matures, academia and industry must increase the pace with which they pursue collaboration that delivers meaningful results. In our discussions with researchers in both academia and industry, we identified a number of factors that should improve the chances for successful collaboration:

- 1 With respect to drug discovery and similar core research, Pharma will need to adapt itself culturally to take on a much more direct collaboration with academia, especially with respect to how academic research activity is perceived and how the different skill sets of the two can best complement each other.
- 2 Opportunities abound for Pharma to participate in research that is ancillary to core developmental research but which creates or improves the tools required to promote translation (eg bio-marker identification).
- 3 As academia pursues development further down the pathway, Pharma will need to reassess its position on how it manages risk and supports research at earlier stages than traditionally preferred, which will require them to consider new ways of sharing commercial rewards.

4 In particular, as the lines along the developmental pathway become crossed between academia and industry, the issue of intellectual property ownership will become critical, offering an opportunity to those companies that prove most flexible and innovative in their approach to collaboration with academia.

5 Collaboration must include the capability to bring together the right parties to form optimal project-specific partnerships, and the overall approach must incorporate a disciplined process for managing the portfolio of opportunities to the potentially divergent benefit of both parties.

These five factors constitute the most critical issues highlighted by those we interviewed. Industry players would find competitive advantage by responding to the opportunities translational research offers, especially within the evolving role of academic medical research. Collaboration has been shown to be the key theme in surmounting the challenge, and the five factors we have outlined form the core of what future collaborations should look like. Above all, by establishing mutual respect among all researchers engaged in collaboration between academia and industry, the path is prepared for identifying and pursuing potentially exciting new medical challenges in translational research. **DDW**

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