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editorial

Chris Molloy

Drug discovery tomorrow: how to Catapult ourselves into the future

The changes in our industry are as exciting as they are challenging. The changing roles of pharma, biotech, the service sector and charities combine with patient and payer pressures to create the need for higher value, precision medicines. In the future a more complex mixture of agile companies will be working in partnership to generate targeted medicines, founded on real world patient data, accessing stratified patients at an earlier stage and using more complex biomarkers and diagnostics to measure their impact. However, this will not happen by itself. It will need energy, expertise, collaboration and a long term view.

The Medicines Discovery Catapult has been created to support the community on the journey to that future. Its facility at Alderley Park, Cheshire, provides a fragmented sector with a place to work together, access to scarce assets and to de-risk their new prototypes and services. Its strategic initiatives link the industry with national stakeholders to provide new foundation processes, and its collaborative projects with industry and academia establish proven new techniques and technologies. As its name implies, it is a store of energy, and a resource the sector can use to propel prototypes and products towards commercialisation.

High value precision products needed

The recent debate over the cost of bringing new medicines to market highlights three main issues. First is the impact of failure: which sends the unit cost of any new marketed drug spiralling from $700 M to over $2bn [1]. The second is time: the 10+ years that it currently takes to get medicines to market soaks up capital and often causes projects to be shelved due to changes in big pharma business strategies. Finally, even the $700 M cost for a new medicine is becoming insupportably high, particularly for more targeted, niche medicines: a commercial point seismically made by incoming GSK CEO, Emma Warmsley [2].

These truths demonstrate the need for high value products. These are products that real patients want, combined with the measurement of their impact to those who pay. Just as changes in industries such as automotive, engineering – and even retail – have required more precision approaches to deliver high value – so too for medicine.

We need to put the patient at the beginning, become more predictive in pre-clinical testing and develop means by which to safely access stratified patient cohorts at an earlier stage. This will reduce large scale clinical trial failures that cost the money and take the time, which the sector can no longer bear [3].

Putting the patient at the beginning

Whether one looks at the world from an 'experience of disease' or takes a biomolecular view, one thing is true: the answer is in the patient. The work done by groups such as Faster Cures in the USA and the Association of Medical Research Charities (AMRC) in the UK are part of a movement to put the patient first.

It is still the case that product profiles new medicines exist behind the walls of big corporations and may only reflect one manifestation of any disease. There is best practice shown from organisations such as the Medicines for Malaria Venture (MMV) where desired product profiles are refined by experts and published on behalf of the community. Charities can be helped to provide

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more of patient-centred profiles, which will allow innovators to produce new products not just for the primary disease, but also those elements that are often overlooked. For example, in Alzheimer's disease a product profile can be developed for a range of symptoms including agitation, which is a key element of a patient's experience of disease, but is not reflected in worldwide R&D pipelines.

New diverse businesses models

Over the last 10 years the sector has become more 'externalised' and networked than ever before. The industrial use of academic drug discovery and clinical academia has increased markedly. In addition, the role of contract researchers has become much more that of a true research partner. However, biotech business and funding models lack diversity. The upstream integration of biomarker and diagnostic companies with therapeutics biotech's also remains low; and young digital companies – who could make a massive impact – find it hard to penetrate an industry seen to be set in its ways.

Companies with new technologies, radical approaches and novel thinking need to be nurtured, not moderated. Innovation does not always work but without the willingness to support the effort required, it will certainly fail. Long term systemic change is also needed and can be supported by the public sector, as has been seen in the UK with the Cell and Gene Therapy Catapult and in the USA through the National Institutes of Health (NIH) and the Defense Advanced Research Projects Agency (DARPA).

New technologies and processes: independent evaluation and application

New companies will bring potentially enabling technologies to bear from academia or outside the sector, and will need more than funding to prove themselves. Critically it is the combination of innovative ideas and expertise that makes for success. At the same time the sector, and the wider stakeholder groups of pharma, regulators and the service sector will have to understand where these technologies will show value. This often requires an independent, honest broker to shoulder the burden of proving principal with a technology. This used to be done by pharma who had both the budget and a strategic interest in technology development. Those days are (mostly) gone and it is therefore all the more important that bodies like the Catapults pick up the baton for application testing and development so that the sector benefits as soon as possible from workable ideas.

New data

Medicines Discovery has always been fundamentally a data science, and is increasingly recognised as such. To put it simply: **the group that understands the data best wins**. Every experiment generates multiformat data and every decision point uses it.

In tomorrow's model the pharmaceutical, biotech and diagnostics players require high levels of information readiness before they start to develop prototypes and products. However, these data skills are often absent in industry veterans and those who understand the regulated process of medicines R&D. Even if some advanced data understanding is present, SMEs are often too small to leverage it. For this reason, it is vital that young, data-savvy companies are nurtured, and mix with the biotech and services sectors.

Catapult: laying stepping stones towards the future

Enter the Medicines Discovery Catapult. This not-for-profit firm has recently been established as a national facility for collaborative medicines discovery. Funded by Innovate UK, an agency of the UK government, it brings together fragmented groups of industry, academia, charities, technologists, services and finance companies who together can turn good science into new, high value medicines. It supports new approaches to the discovery and proof of precision medicines, diagnostics and biomarkers.

Headquartered at Alderley Park, UK, it is collecting a broad range of rare scientific, informatics and industry skills; and providing expert access to scarce new technologies that the sector really needs today. It is also enabling research charities through a new, joined up consortia called Discovery Syndicates that will engage patient groups with industrialists and academics in bringing the highest value, targeted treatments to a successful proof of principal in redesigned clinical trials.

It has four major themes;

- Helping de-risk and prove new technologies and scientific models
- Providing industrial expertise and smoothed access to the CRO network for SMEs, academics and charities
- Helping develop and prove new processes and regulatory pathways to efficiency
- Make more national assets of patient samples and data safely available to the SME community

The Catapult is there to do the things that others in the sector are not able to do by themselves, and will not be in competition with its community. It is always listening for the phrase ''somebody really needs to . . . '': the trigger expression of a sector requirement for collaborative help. It can therefore be thought of as a national workbench for trying and testing new approaches, technologies and processes in a secure, safe and expert environment.

What does the Catapult do?

The Catapult has science, informatics and collaborative project work at its heart. The teams will not be replicating the activities the sector can already do, like standard pre-clinical testing and standard clinical trials. Quite the opposite. It will be working on high to medium risk projects that the sector cannot yet do, or would like to try. This is shown in its early investment in new modes of mass spectrometry, solid state NMR drug-target interaction, and it has now opened up to the SME community and its work in microbubble drug delivery. There are also plans to invest in complex cell system technologies to improve how we predict the efficacy – as well as safety – of new medicines going into patients.

In informatics it will invest in the generation of systems that will help the community access available real-time data and sector knowledge for earlier decision-making on discovery approaches and improve the interoperability of systems and data that today rarely interconnect. All to enable the community to work better together.

The Catapult will also be creating a nationally available platform for discovery project externalisation that will enable SMEs and translational projects to access 'pharma-class' level of industrial programme management, expert CRO networks and specialised academic assets, along with a strong informatics

backbone. This will involve the creation of a national network of drug-hunting experts whose experience will enable the projects to do the right experiments to make their prototypes industry consumable and financeable.

Finally, the Catapult is already working with SMEs to get better, secure and consented access to patient samples and data. Working with national stakeholders it aims to help the community to identify what assets are available and help broker the right deals to enable more rapid testing of prototypes and the de-risking of patient-centred innovative approaches.

The Catapult's ''Discovery Syndicate" concept also opens up radical new ways of translating good science into good medicines. The Syndicates will be long-term discovery consortia – anchored by disease-specific medical charities – that will contain biopharma SMEs, technologists and larger companies with a focus on that disease. Charities bring to the Syndicates a greater visibility of clinical realities and real unmet patient needs; the industrial players provide a clear view on the areas where collaborative R&D will overcome technology and process barriers. The Catapult will manage the consortium process and provide the framework for the R&D to occur, both externalised through the CRO community and within the Syndicate. Some proof of principal models already exist in some diseases, such as cancer (Cancer Research UK) and with some large public-private funds, such as dementia and the LifeArc Communities for Impact. New models like this put the patient at the beginning of discovery. They also provide extra robustness and variety to the environment.

The precise route to a precision future is not known. However, the nurturing of a more complex supply chain of agile, diverse companies will enable the UK to adapt to the changing behaviour of multinational pharma and will enable the translation of patient need into targeted medicines and precision diagnostics. The Medicines Discovery Catapult is open for business and actively working with industry and charity groups, large and small, who have already voiced the 'somebody really needs to'. By sharing problems, rare expertise and assets it will support the growth of this new community, which is a future we can all look forward to.

References

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Chris Molloy
Medicines Discovery Catapult, Block 35, Mereside, Alderley Park, Alderley Edge, Cheshire SK10 4TG United Kingdom
chris.molloy@md.catapult.org.uk