Interview: Chris Molloy â?? Chief Executive, Medicines Discovery Catapult (MDC), UK

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Chris Molloy, chief executive of the Medicines Discovery Catapult (MDC), discusses its role within the UK as a center for applied medical R&D and the future of the countryâ??s drug discovery profile post-Brexit.

Could you please start by introducing the MDC?

The Medicines Discovery Catapult is one of 11 catapults in the UK, each of which focuses on a particular industry vertical. Each Catapult acts as a center for applied research and development, acting to clearly address the barriers that industry vertical faces. The Catapults bring together consortia of academics, technologists and industrialists. Through applied research and development, they create new products and services that can be absorbed by the market to assist the growth and development of that particular industry vertical. The MDC aims to assist the UK small and medium sized entities (SME) community in their current growth, development and funding while also helping them adapt in preparation for the future of the drug discovery sector. The process through which the Medicines Discovery Catapult achieves its aims is by assisting the community at every stage from the creation of a new idea for a medicine, through to the point at which the medicine is proven for the first time in a patient. The MDC community is comprised of translational academics, biotechnologists, contract research organizations (CROs), large pharmaceutical companies, and technologists. We are headquartered in the former AstraZeneca research and development facility in Alderley Park in Cheshire. Our core funding is derived from Innovate UK which is part of UK Research and Innovation (UKRI). However, we gain additional funding through collaborative

research and development grants while also benefiting from industrial revenues.

What are the MDCâ??s main capabilities?

It is important to consider that 60 percent of safe molecules that we put in to first in-patient studies, fail. However currently 60 percent of molecules that enter phase one succeed. We have improved significantly through the application of technology and due to our focus on improving our success rate in terms of understanding safety. Our current aim is to extend this efficacy, particularly in relation to diseases that are deemed to hold a significant risk factor. We are especially focused on diseases that have seen many of the larger companies move away. For example, neurological diseases, metabolic diseases, diseases centered around inflammation and musculoskeletal disorders have all faced these challenges.

We have four basic capabilities; the first of which concerns discovery science and technology. We have a team of industrial and academic scientists, who understand the ways in which new technologies must be proven, and the preclinical research models that are industry rigorous. That team are being utilized by our community to translate, validate and disseminate new cellular models of disease and advanced ways of measuring them.

Our second significant capability relates to informatics. Today, we have more access to data than ever before in human history. Therefore, it is a necessity that we take a scientific approach to link data sets and systems together. This will allow us and the SME community to translate, validate and use new algorithms, informatics methods and data mining approaches to improve the predictability of our pre-clinical and clinical research.

The third element of our capabilities is related to virtual research and development. This is the use of multiple private and public-sector capabilities to run â??outsourcedâ?? research and development projects but underpinned by industry rigor. Large pharmaceutical companies have gained significant expertise in this approach for drug discovery. However, many SMEs have limited experience of which experiments needs to be run, where they are best performed and how to run these complex projects efficiently. Our platform aims to address that by harnessing two essential capabilities; firstly, we are harnessing those human resources through the formation of a national academy of drug discoverers which can be deployed in order to assist SMEs in determining which experiments need to be run. Secondly, we are harnessing the national capability in conducting experiments through CROs and specialized academics. If these aims are achieved sufficiently the result will be the provision of a â??National Help Serviceâ?? for translational SMEs which will increase efficiency of translation. This efficiency could mean successes are achieved at a faster rate or rather that programs are finished before they result in costly failures at a later stage.

Our fourth capability is the ability to provide SMEs with easier access to consented patient samples and patient data. 75 percent of SMEs use sources outside of the UK in order to access these resources. However, the UK has an excellent resource of consented patient samples and patient data. Our work focuses on reducing the barriers surrounding the contracting of and access to these consented samples and patient data.

Overall, these four capabilities are held together by a single vision, which is to put the patient at the heart of discovery.

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What motivated you to join the MDC?

I was motivated to join the MDC by the experiences that I have gained throughout my career. Over 28 years I have gained experience in large pharmaceutical companies, biotechnology, life sciences, informatics and the development of strong executive teams. The MDC brings these areas together. In particular, we aim to utilize our understanding of what rigorous drug discovery requires, the vital importance of technology, the omnipotence of data, and the necessary requirements of putting the right people in the right places at the right time.

What research and development projects are currently being undertaken by the MDC?

The MDC is a relatively new organization. One year ago, we were comprised of only four people; we now have 58 people, so we have grown more than ten-fold in just under a year. Nevertheless, we have already had a significant amount of sector engagement. We have had engagement in two main areas; one is the development of better discovery â??modelsâ?? and the other is the improvement of translation methods. In regard to better models we are working on the new generation of patient relevant or patient derived cellular models and data models. These systems aim to mimic the human disease condition more effectively and therefore select drug candidates more predictively. In order to do so we are working on microfluidic-based Organ On A Chip systems. We are also measuring the cells in exquisite detail using advanced mass spectrometry that measures the chemistry of cells and tissues in almost â??real-timeâ??. These emerging techniques need our work to make them as robust as industry requires so that they can be widely adopted.

We are also currently working on a new model of drug delivery which uses micro-bubbles. This project acts to translate technology developed by the University of Leeds. The technology is a cross-disease technology which allows for a new method of very precisely delivering drugs to a particular location within the body. This â??drug cargo systemâ?? can be tracked and triggered using ultrasound. This is particularly useful if for example a patient has a particular tissue to which a drug needs to be located. A targeting mechanism can be attached to the bubble which can then be triggered by an ultrasound machine which acts to explode the bubbles thus allowing targeted delivery of drugs. This in turn can enable the repurposing of certain drugs that might otherwise have a particular toxicity or efficacy profile which would render them unsuitable when delivered using alternative methods. Thus, it is a cross-cutting, cross-disease technology.

Despite being at a relatively early stage in our development as an organization we have a number of promising projects being undertaken. We are currently communicating with a vast number of SMEs in the UK in an effort to develop faster translation in order to further develop the pipeline of high impact R&D.

Please tell our readers about your disease Syndicates initiative.

Our initiative aims to discover new ways of collaborating in order to generate, test and prove new drugs. Currently a large number of venture backed companies are single asset companies. While single asset companies can be successful, they pose a higher risk in regard to drug discovery. Thus, we support the development of new consortia with a portfolio approach which poses a lower risk to drug discovery. A portfolio of medicines centred around a single disease also increases efficiency, as the portfolio will likely follow a similar set of pathways in order to go from the idea to its clinical proof in patient trials.

Furthermore, if that consortium is then cornerstoned by a research charity there is further opportunity to unlock the potential to bring medicines to market faster for patients. Charities in particular have the immense advantage of patient trust. For a long-term effort such as drug discovery, a long-term anchor point is a necessity, and there is no better long-term anchor point than the patient. Research charities have an in-depth understanding of what real, unmet patient needs are. If that consortium

can then involve SMEs and larger pharmaceutical companies. This represents a lower risk, long-term approach that may attract, longer term impact investment.

The traditional form of financial syndicates are generally consortia with capital seeking risk. Our model is a disease Syndicate is a consortium of R&D risk seeking money. Money is generally more attracted to disease causes than scientific causes. Thus, there is the potential for a highly efficient, mutually beneficial, increasingly long-term, and lower risk model.

Despite the numerous advances made in biological sciences over the past 50 years, productivity has fallen for decades. On average top drug developers now register a return on investment of nearly 3.4 percent. What are the driving factors behind this depletion in productivity? And how are these issues being approached by industry?

There are a variety of reasons for this reduced productivity. The increasing complexity of the medicines being developed and manufactured, is in part responsible. The return on investment in larger companies is also influenced significantly by the extent to which assets are developed internally in comparison with the extent to which companies license them in from elsewhere. Various companies are taking different approaches to the problem of declining productivity. While some are taking particularly commercial approaches in accordance with the market, others have explicitly taken a policy of following the science.

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Are there similar initiatives to the MDC being enacted in countries outside of the UK?

With our focus on proving new technologies and assisting SMEs in progressing their ideas efficiently the MDC is unique in the UK. However, there are similar organizations in Europe, such as The Fraunhofer Institutes in Germany. Overall the model is certainly a European invention, if not a specifically British one. There are a few companies starting in the US, co-funded by industry and venture capital that seek to help progress their assets, but they do not share our technology validation support model.

A few words to conclude?

The overriding issue the drug discovery community has in relation to Brexit is uncertainty. However, I have no doubt that the agility of the UK community, the wealth of its science and the strength of its financial industry, can and will provide the next generation of biotech companies, who will without doubt maintain strong relationships across Europe and around the world. These relationships are long lasting and have been built on strong traditional, personal and professional linkages. These linkages will maintain the global nature of the process of identifying and providing new drugs. Nevertheless, the UK has the opportunity to harness its national resources in order to become the location in which companies wish to establish and grow discovery biotechnology programs.

The UKâ??s national infrastructure and resources enable that. The MDCâ??s role, as a lightning rod, is to make sure that those resources are targeted efficiently, and that they are available to the right companies at the right time. Through Brexit we hope to be a neutral broker in this process in order to achieve our aims and vision.

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