Keith Thompson – CEO, Cell and Gene Therapy Catapult, UK



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Keith Thompson, CEO of the Cell & Gene Therapy Catapult, one of a number of Catapult institutions in the UK designed to help commercialize innovative research, discusses strategy, funding, international collaboration and Brexit.

Could you please explain the concept of the Catapults in transforming the UK's capabilities for innovation and taking on challenges that are too complex or risky for individual firms?

The whole Catapult idea came out of work done through the late 2000s. When the coalition government got in in 2010, they undertook a number of measures. Number one, they maintained the science budget, when everything else was being cut. Secondly, on the basis of the issued reports, they asked the question which has been asked over and over again in the UK which is, "Why are we so good at inventing things but failing to fully exploit those discoveries?" And that is a very complex question. I think the UK is good at making its inventions stick. Nevertheless, a gap was identified which is the intermediary technology institute – the Catapult, in-between industry and academia that would help accelerate innovation.

The rationale at the time was that there were a number of tests for establishing Catapults: is the UK science base really good? Is there some form of market failure where the science base isn't getting out into industry for whatever reason or as efficiently as it might do? Does the UK economy have the capacity to absorb the outputs of the Catapults? Could the type of work that a Catapult would do accelerate the growth of that industry and make it stick? If you look at all of those tests, cell and gene therapy meet them all very easily.

If you characterize the industry of 2012, it was the preserve of academia, a cottage industry, a few pioneering companies, and there was no traction from major investors or big pharma because there was no established route by which you could ever see these potential discoveries getting to market.

The question I asked was: "If the science is so good, what are the barriers to its development?" I set up the catapult to address those three main barriers. There was a technical barrier involving how you make these products and how to turn a cell or a gene into a medicine that can be delivered (because you cannot simply put cells into blister packs and sell them at the pharmacy!). The second was how to get it through regulation and clinical trials when it is so different, a lot of people at the time were trying to reverse cell and gene therapy into a biological paradigm but it needed regulation appropriate to the science. And lastly, there were business barriers asking for clarification of the business model and how to pay for cures.

We therefore set up the first facility from scratch, located at Guy's Hospital in London; we recruited the teams that would occupy it and then at a later stage, we decided to build a large-scale GMP manufacturing facility to address those barriers. I put together a clinical and regulatory team who were experts with management from the pharma industry. I put the technical experts together that would know how to industrialize the academic processes.

This is one of the big aims of the *Life Sciences Industrial Strategy*. The big questions were how to scale and industrialize? How would you go from this cottage industry to an industrialized manufacturing process that was capable of being licensed and cost-effective? At the time, the understanding of economics was virtually absent from the entire field. So we started a health economics unit at Guy's as well.

We either worked with some of the existing companies help accelerate their products, or we went to the university base to get a few pathfinder projects and deploy all our expertise on them. By doing that, we were breaking those barriers down, and have been very successful doing so. Along that process, we addressed the complex labyrinth of regulation that existed in 2012. Now there is a

single, one-stop-shop run by the MHRA. All the time scales have reduced and proportionate and effective regulations are now in place. Most likely, the UK is the best environment for putting forward trials that are properly regulated. Initially that tipped a lot of venture capital into the field, but obviously now there is a lot more corporate capital coming in too, which is exactly what we want.

What levers, mechanisms or capabilities do you have today to address those three barriers?

We still essentially have the same three legs of the stool. The regulations are an awful lot better although they haven't gone away; the scale-up is moving from going through a continuum now and we have divided our programs into a series of waves. One of them is called 'intelligent manufacturing', which is about taking these processes through the initial stages to making them efficient and going from small-scale to large-scale automation. We have another wave moving forward called 'gene delivery', which is about improving viral vector processes. But it is also about non-viral gene deliveries as well. We are looking at areas ranging from electroporation to nano-particle delivery, which would absolutely revolutionize the whole space. Also, we have a 'supply chain' wave, which essentially is our new big manufacturing centre and the development of the supply chain out in Stevenage.

We started off with cell therapy. We were always involved in gene therapy, but it progressed a lot faster than we thought it would. We added it on, because at the time when we first started we hadn't really recognized that aspects like viral vector supply would be an issue. We built a small viral vector group, and now we have some of the best analytical methodologies coming out in some scale.

Developing that manufacturing supply chain is very important. We identified this gap in 2013. There were in the UK many well-supplied, small-scale academic facilities but if a project was successful they did not have a facility where they could scale up. We therefore proposed that a large-scale GMP manufacturing facility be built, with a series of large-scale clean rooms that could accommodate large-scale processes. Fortunately, I was able to persuade government to back the idea and invest in it. Then, we would provide an entire wraparound of expertise from process development through to management. We would subsequently have well-invested companies come in to run their own processes in there.

The facility is technically designed to allow processes for large-scale allogeneic manufacture, up to a thousand litres. It can accommodate autologous manufacturing of cells, for multiple cells – i.e. patient-specific – with multiple batches in one clean room. And it can also accommodate viral vector processes again up to a thousand litres. There are very few that have gone beyond a thousand litres. It truly is a large-scale facility and we've built out the first six clean rooms. We also recently received funding through the Industrial Strategy Challenge Fund to develop the second floor of this building with a further six, even larger modules. Finally, it has full commercial-scale quality management system and other systems such as warehouse management. We collaborate with companies that do tracking and tracing; we also capitalize on having the Stevenage BioScience Catalyst and GSK alongside us. GSK has its main cell and gene unit and there are several cell and gene companies that are in the incubator units in the Stevenage BioScience Catalyst. It is probably has the highest density of industrial expertise in one location, certainly in Europe and possibly globally.

Where does your funding income come from?

The first funding we received was GBP 70m, to start our operations in London funding both our labs and technology pathfinder projects. We then obtained a further GBP55m for the Manufacturing Centre the majority of which has gone on capital and systems and deploys some of the technologies that we have developed or are developing. We recently obtained another GBP 12m from the Industrial Strategy Challenge Fund. So, we are talking of a current envelope of GBP 67-70m in the manufacturing centre.

Our funding essentially comes from three streams. The core grant comes from the UK's Department of Business, Energy & Industrial Strategy (BEIS) which goes into UKRI and Innovate UK, and then, it comes to us. It allowed us to establish infrastructure and expertise ahead of where the industry is. The next stream of grants that we get are by winning collaborative R&D projects. Many of which are from Innovate UK or the Industrial Strategy Challenge Fund. Some of them are with the Wellcome Trust, the Medical Research Council (MRC) or Horizon 2020. The last bit of money we get is straight-forward commercial work leveraging our unique assets. Eventually, two thirds of the money will be independent of the core funds.

The Catapult funding model is sometimes called "a third, a third, a third." The initial third is all about establishing the technological capability, refreshing it and growing it so that it can then be accessed through collaborative R&D or commercially by companies. That whole idea of leveraging

an investment through these other mechanisms really works, and I think this is one of the underlying and key parts of the infrastructure. It allows the Catapults to be industry-led which is very different to other technology innovation models that exist. There are innovation research organizations in other countries, but most of them are in some way attached to a university and much more academically-led. Here, we are industry-led.

An MoU with the Japanese Society for Regenerative Medicine (JSRM) was recently signed. What was the idea behind that?

All our work is centred around the idea of accelerating the development of an industry in the UK, whereby manufacturing will be crucial. I strongly believe that having a manufacturing supply chain roots an emerging industry into the economy and is important for its longevity. For Cell and Gene Therapy it is not just R&D that then filters out to existing supply chains. When you establish new manufacturing and supply chain assets and expertise, the roots go down making it hard to move and creating clusters of expertise. There is full recognition that we are in a global industry as all healthcare is. We recognize the fact there are big players in the US, Japan and China, and we have worked hard to establish links with both the Japanese system and Japanese companies. We hired a first-class Japanese molecular biologist to work with us and a full Japanese experienced team. As it tends to take time to build up relationships with Japanese firms, we thought we would sign an MoU with JSRM, along with FIRM and the Kanagawa Prefecture. They have been crucial is giving solidity to our relationship.

As drug development is becoming increasingly global, what do you see as the effect of Brexit to your endeavours and Britain’s place of being a leader in cell and gene therapy?

Cell and gene therapy has been nurtured in clinical research rather than university science, and there are several good groups across the UK. A huge concentration is in London, but there are centres scattered all the way up the UK to Edinburgh and Glasgow. I think that once you get past Brexit, all the fundamentals are here: the good science, the clinical research, the excellent regulatory environment, and an industrial strategy from government which has put its money where its mouth is and supports the translational research.

The UK’s strengths are in early clinical results, real life clinical outputs, and it’s the knowledge and know-how of how to manufacture and move product. The UKs ambition is to do that better than anyone else, and that will not change, it’s not just in cell and genes, but a huge portion of Europe’s medicines are quality-controlled and released in the UK. Anybody who thinks they are going to put barriers up – which means that their populations are not going to get timely availability of medicines – are probably making a big mistake, whether they are British or European politicians. Theresa May only last week asked for MHRA-EMA affiliation and that’s what all stakeholders in the UK desire. The MHRA has historically played a very influential role on the EMA. Something like 40 percent of all approvals have come through the MHRA.

A few words to conclude?

I think there are two matters to conclude on. This whole sector – cell and gene therapy – is seen as the “up and coming” area in life sciences. But it is beyond “up and coming”, it is here today with approvals happening now. Gene therapies, and gene modified cell therapies for certain blood cancers are here and they are going to be moving forward into the hospital environment now. We have a big initiative with Innovate UK to establish specialist treatment centers for advanced therapies across the country.

The second real point in that is that we are now, as the Catapult, entering our second five-year program where the fantastic assets that we have built will continue to help accelerate the UK as a leading force in cell and gene therapy.

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