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The UK Biotech Sector and Brexit: Past Performance and Future Prospects

Sir Geoffrey Owen and Dr Michael Hopkins

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1. Introduction

"Given that we are on the doorstep of one of the world's great financial centres, there has been a paucity of risk capital for life sciences … We've never had a Gilead or a Celgene [in the UK] and this is becoming a pressing issue." Sir John Bell, Professor of Medicine, University of Oxford.

Taken from an interview with *The Financial Times* (Ward, 2015), Bell's concern about the status of the biotech industry in the United Kingdom (UK) is heard repeated by many in policy discussions throughout the country. Bell would be the first to acknowledge that the lack of financial funding is not the only causal factor. This seminar briefing examines three aspects of this issue: (1) why the UK has not produced large biotech firms that develop drugs, similar to those in the United States (US), (2) why the UK biotech firms that do exist have not brought blockbuster drugs to the market and (3) what the implications are for industrial strategy after Brexit. These remarks are based primarily on research we completed for our recent book, Science, the State and the City (Owen and Hopkins, 2016), with some additions and specific observations about the potential effects of Brexit.

2. What is the Secret to US Success in Biotech?

Many countries have attempted to emulate the US innovation ecosystem, not just for biotech or the life sciences, but all sectors. The US approach has created several large, high-tech companies

able to draw on substantial resources, produce radical innovation and be profitable. Not only have attempts to emulate US success failed, but the US actually has increased its lead over the past 40 years. Why is that? What is the secret to US success?

No one factor is responsible for the US lead in biotech innovation. A mix of factors is at play. Some probably cannot be imitated by countries much smaller than the US. Four key sets of factors we identified in our research include, first, the capabilities of the local firms involved. Partly because of its size, the US has had a greater concentration of a broader range of some critical capabilities. Second, particularly in terms of biotech, timing has been critical. In the US, important institutions essential to supporting the emergence of the US biotech sector were established, for other reasons, long before they were needed for biotech — but they were in place and ready to go. In the UK, in comparison, we needed to build those institutions at the same time we were trying to build the sector. As a result, the sequence of events was sometimes out of order, affecting the growth of the sector.

A third factor in the US success in biotech is scale, an important critical mass. Specialization and an effective division of labour depend on scale. The US has a large health care market and extensive funds for investment, both of which have been essential to creating or encouraging essential expertise and consistently generous funding. This has been difficult to do in other parts of the world, not only in the UK. The fourth and final factor is that the effort was further enriched by interaction between the biotech sector and other sectors — e.g. academia, venture capital, the traditional pharmaceutical industry and various ancillary entrepreneurs. By the time the biotech sector began to emerge in other parts of the world, the US already had become the leader and the world's centre of biotech activity.

3. Data and Insight

In exploring how these factors have contributed to success in the US and a lag in the UK, we drew on a range of materials. First, we explored the substantial body of grey literature on the development of the biotech sector. Each of us already had an impressive collection of reports, papers and books gathered over the years. The Science Policy Research Unit (SPRU) at the University of Sussex also has an extensive library.

Data on UK firms came in part from a prior project that had developed a database of 247 UK biotech firms, most of which founded in the UK, that had an interest in drug development (see Hopkins, et al., 2013). We built on that data and also drew on data from other sources such as Nature Biotech, which publishes an annual summary of the sector each year.

We were not the first to explore some of these issues and we benefited from the numerous studies of the history of biotech, many from scholars in the US (e.g. Orsenigo, 1989; Bud, 1993; Achilladelis, 1999; Casper, 2007; Hughes, 2011; Powell and Sandholtz, 2012; and Marks, 2015). We also conducted interviews with colleagues — primarily in the UK, but also in the US, France, Switzerland and, remotely, Japan. The focus of questions in the UK included how the sector had evolved, what limitations it had faced, etc.

4. The Emergence of Biotech

The story starts, in our telling of it, with the emergence of two key biotech techniques in the 1970s: recombinant DNA and hybridoma to produce monoclonal antibodies. These were what initially

attracted serious interest in drug development based on biotech and created the new therapeutic biotech sector. These new companies were set up by new entrepreneurs, not as extensions of existing pharmaceutical companies. Interestingly, the breakthroughs on these two technologies occurred on opposite sides of the Atlantic: the key advances in recombinant DNA technology were the result of work in San Francisco by Cohen and Boyer; the breakthrough advance in the hybridoma technique that facilitated the production of the first monoclonal antibodies was the result of work by Milstein and Köhler in Cambridge UK.

Genentech, founded in the US 1976, was not actually the first biotech company, but it became the "poster child" for the sector. Genentech applied recombinant DNA technology to produce insulin faster and more efficiently than had been possible using extraction from animal sources. The company was formed with the support of local venture capital in the San Francisco Bay area, and in less than a decade the company had been listed on the stock exchange and formed an alliance to market its insulin with a leading pharmaceutical company.

The time between the development of the technique and the actual launch of a monoclonal antibody drug was much longer — 20 years — because it was a more complex technology to apply in practice. Even though the breakthrough had occurred in the UK, the first monoclonal antibody drugs were brought to the market by US companies. The UK had not been able to take advantage of the lead it had in knowledge to retain the lead and produce the first marketable products.

Table 1 shows that US biotech companies were successful in bringing a number of products based on recombinant DNA to market by the end of the 1980s. The list is not comprehensive, but it does demonstrate not only that Genentech continued its success with a series of products, but also that several other biotech companies marketed new products — and for indications in lucrative markets such as cardiovascular disease and cancer. The success of these products attracted even more investment in the industry, producing a virtuous cycle of investment and commercial success.

Table 1. Early US biotech therapeutic successes

Product (brand name)	**Company (partner)**	**Indication(s)**	**Year**
Human growth hormone (Protropin)	Genentech	Human growth hormone deficiency	1985
Interferon-alpha-2a (Pegasys)	Genentech (Roche)	Cancer, viral infections	1986
Interferon-alpha-2b (Intron)	Biogen (Schering-Plough)	Cancer	1986
Hepatitis B vaccine (Recombivax HB)	Chiron (Merck)	Hepatitis B	1986
TPA (Activase)	Genentech	Cardiovascular disease	1987
Erythropoietin (Epogen)	Amgen (Ortho)	Anaemia	1989
Interferon-gamma (Actimmune)	Genentech	Cancer, infections, inflammatory diseases	1990

Source: Selective list from Grabowski and Vernon, 1994

A few decades on, the largest firms in the biotech sector have become at least as large as established pharmaceutical firms. Initially, only Genentech and Amgen were major players; now a number have high valuations — Alexion, Biogen, Celgene, Gilead, Regeneron, Vertex. A few companies, e.g. Genzyme and Genentech, already have merged with or been acquired by established pharmaceutical firms (Sanofi and Roche, respectively). The US, in short, has produced several important biotech companies — and dozens more of lesser valuation.

If we compare the success of the sector in the US with that in Europe, the lead of the US is striking. With about 500 million people, Europe has a GDP of about $16 trillion; the US has 325 million people and a GDP of about $18 trillion. Nevertheless, the US has about two to three times more public biotech companies listed on the stock market than does Europe. The market capitalisation of those US companies is just under ten times that of the European sector. Turnover is seven times greater and US biotechs raise about eight times more capital from initial public offerings on the stock market. These are impressive differences.

5. Sources of Success in US Biotech

Many researchers have attempted to identify the reasons for the success of the US in biotech (see e.g. Henderson et al., 1999; Prevezer, 2001; and Nelson, 2008). The critical factors are as follows.

1. The US has invested heavily in biomedical research for decades. That means that a greater number of potential avenues exist for research leading to discoveries that are later commercially viable. It also produces more post-doctoral trained scientists than the academic system can absorb, and who thus are available to be hired by biotech companies.

2. As noted above, the US addressed important institutional issues early on. For example, a court case in 1980 established that recombinant organisms that could produce insulin and growth hormone, for instance, could be patented. In the early 1980s, the Bayh-Dole Act encouraged the commercialisation of federally-funded research; and the Food and Drug Administration (FDA) encouraged pioneering research by offering streamlined regulatory pathways for breakthrough drugs and for orphan indications. Although similar provisions were eventually made in Europe, it was considerably later.

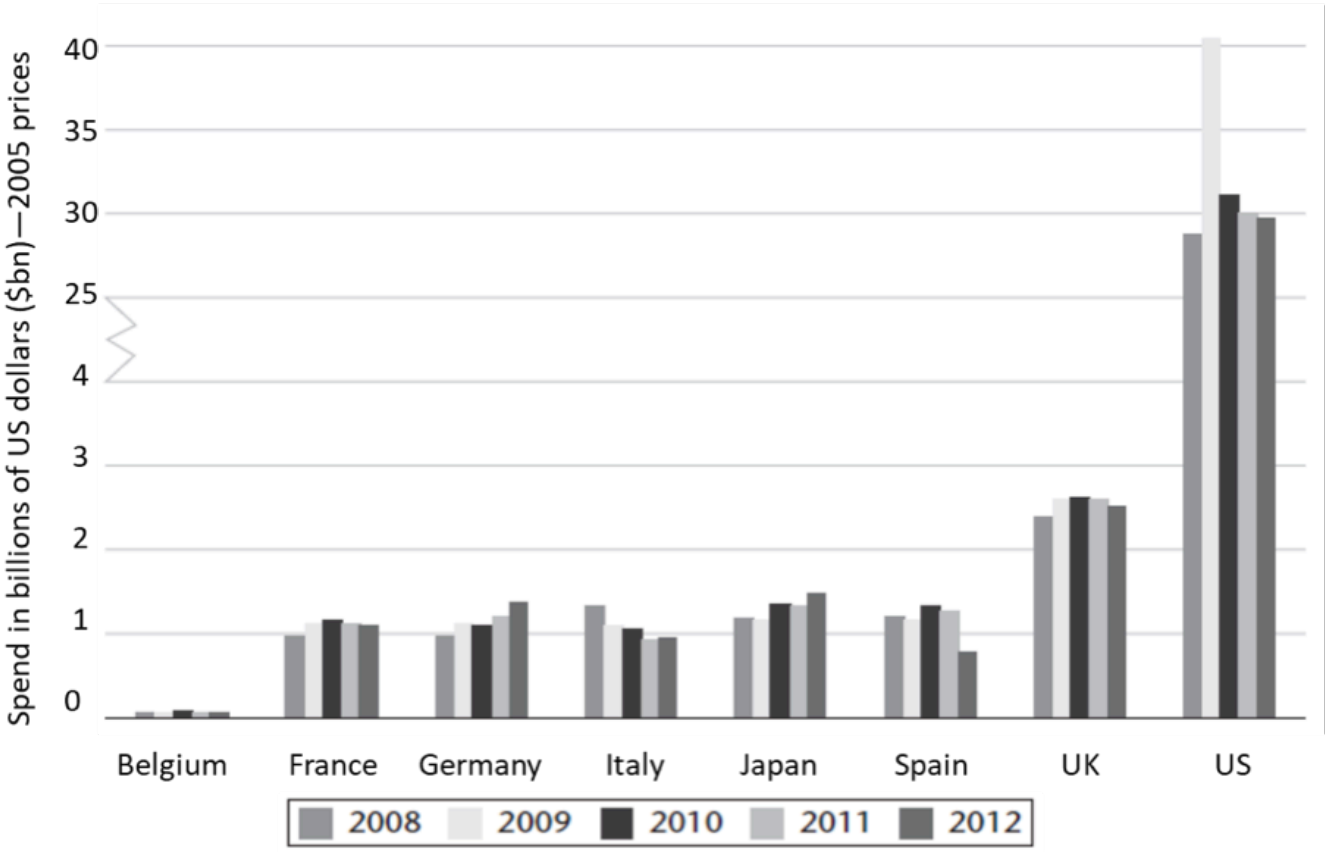
3. The US has a large domestic market, one that is far less restrictive in terms of entry and price than European markets. That allows US biotech companies to rather quickly produce substantial profits, which makes investment in such companies attractive. The US financial markets also are exceptionally supportive of high tech companies, a phenomenon that predated biotech. Venture capital already had experienced success from technological innovation in microelectronics companies, so when biotech emerged, venture capital was predisposed towards investing in this new high-tech opportunity. The stock market in the US is supportive of biotech as well; the NASDAQ has long embraced high tech firms, including biotech. By contrast, the London Stock Exchange (LSE) had rules that prohibited companies from being listed without a substantial profitable track record, something virtually impossible for many biotechs.

4. The established pharmaceutical industry in the US also was a factor in the success of biotech in several ways. Executives from established firms moved to the new biotech companies, bringing important experience in drug development, regulation, and marketing. Partnerships also were important as biotech firms partnered with established firms in completing clinical trials, gaining regulatory approval and effectively marketing their new products in the US and abroad.

Looking in more detail at some of these factors clarifies the sources of US advantage. Figure 1 shows spending on health care by governments in different countries. It is important to note that the y axis here has a break between 4 and 25 to allow the US funding to be shown on the same graph. US spending was about ten times more than the UK overall, even though it is only about seven times larger, so the US is spending more on life sciences proportionately. The spike in 2009 in the US was

a response to the financial crisis: when many other countries were cutting back, the US approved a stimulus package that put an additional $12 billion into the National Institutes of Health (NIH) and required it to be spent within just a short time frame.

Figure 1. Government spending on health-related R&D



Source: Owens and Hopkins, 2016, p. 213.

6. Challenges for Biotech in the UK

UK policy leaders certainly were aware of the activity in the US and many were concerned about the UK's low level of entrepreneurial involvement in the new technology industries that will fuel economies in the future. At the end of 1978, a group was created that comprised British scientists, industrialists and government officials to examine the situation. The resulting Spinks Report, published in 1980, recommended that the UK government found a biotech company (ACARD, 1980). In response, Celltech was established under the Thatcher government. Although Celltech was one of the few companies in the UK subsequently to apply recombinant DNA technology to its pipeline, it did not start out focusing on therapeutics. Cambridge Antibody Technology, founded later in the 1980s, also applied the novel biotechnologies. However, most of the so-called biotech companies in the UK at the time actually were using traditional small molecule chemistry, and just riding the wave of interest that investors had for new biotechnologies.

In the 1980s, options for financing were limited. The UK venture capital industry was in its infancy. Several measures by government were intended to encourage the establishment and the growth of these funds. The financing pool remained quite stagnant until the early 1990s when the LSE opened its doors to biotech companies. In 1995, the Alternative Investment Market was created, which welcomed smaller firms and imposed lower regulatory hurdles. This expanded the opportunities for financing beyond venture capital investors.

Once the financial channels were opened, UK investors enthusiastically funded a wave of companies. What were the investors investing in? We looked at the prospectuses that these companies were using to attract investor interest and we looked at the technologies that were supporting the drugs in their pipeline. What we found was that small molecule drugs still were the major focus; some companies were developing new drug delivery systems — inhalation or slow release — and some focused on vaccines. The UK had relatively few companies using biotech platform technologies like monoclonal antibodies and recombinant DNA, areas that were the drivers of success for the early US biotech companies.

Looking at output, the first 100 drugs that were brought to market by UK firms that benefited from this funding were nearly all new formulations of small molecule drugs. Few were developing biologics or lead compounds that were first in class. Drilling down into the data, we discovered that a number of those biologics were from Shire, which had acquired a US company, Transkaryotic Therapies. The nascent UK biotech industry, then, was mostly based on older approaches, not truly new techniques.

7. Investors Retreat

The enthusiasm and the financial support from the City, which had been high in the 1990s, began to dampen as companies started to report clinical trial failures. Unfortunately, that included some of the firms that had attracted the most attention, such as British Biotech, which for some time in the mid-1990s was called the flagship of the sector. As such failures mounted up, investors stopped making large investments in the sector. Financial activity did ramp up to some extent during the tech boom around the turn of the Millennium, but for about eight years after that no new company was listed on the LSE until Circassia in 2014. Companies during that period relied on the smaller Alternative Investment Market. Biotechs were less able to maintain the liquidity that is needed for shares to be traded smoothly, and often were trapped in a situation where investors could not trade their shares and the value of the companies drifted lower.

During the 2000s, while the US sector was going from strength to strength, the UK market was stalled by the lack of access to capital. The few companies that were successful were bought up either by established pharmaceutical companies in the UK or elsewhere, or by biotechs from outside the UK. As a result, the UK industry began to appear shrivelled and withered—a generation of biotech companies was lost in the UK. A brighter light began to shine again in around 2013 and 2014 when investment in the US boomed and infected the UK enough to prompt the LSE to again be more open. Some companies did receive some funding that way, Circassia being one of those. That company then unfortunately experienced a clinical trial failure during the final phase of research, again casting a shadow over the sector. In terms of financing, then, the US still has a crucial advantage.

Interest in investment continues in the US and the NASDAQ stock exchange is so technology friendly that UK companies prefer a listing there to one on the LSE. A recent example is Nightstar Therapeutics, a gene therapy company spun out of the University of Oxford in 2013. It received backing from and was in the portfolio of Syncona Ltd, the Wellcome Trust investment company. In August 2017, Syncona and Nightstar announced that after long and careful consideration, the company would list on the NASDAQ rather than any European exchange. This was the first public listing of a Syncona-founded company. Both parties are quoted as saying this listing was an "important milestone" in its "ambition of building a global leader in gene therapy for inherited retinal diseases" (Syncona Ltd, 2017). This suggests that these companies see biotech as a global industry, but it also consider the US as the leader — the source of the largest and most sophisticated investors in biotech and where valuation of companies tends to be higher.

8. Following the US Lead

What then made it so difficult for the UK to successfully follow the lead of the US? A read of the pages of *The Financial Times* and reports by analysts who follow the sector repeated identify the short-termism of UK investors or the lack of government support — and perhaps an added element of luck. Certainly, some of the early US pioneers assert that luck was involved in everything going right in the development and launch of their early drugs.

We disagree that short-termism or lack of government support explain why the UK has fallen behind the US. Instead, as noted earlier, the key factors are capabilities and timing. The US had greater access to recombinant DNA technology expertise; talent was available to move into companies in the early years. As it happened, recombinant DNA technology led to highly profitable drugs faster than did monoclonal antibody technology; the revenue from those earlier successes then could be invested in applying monoclonal antibody technology.

The UK companies faltered also in part because institutional structure was built so slowly — venture capital, stock market access, technology transfer regulations. As a result, the first monoclonal antibody drugs that were developed in the UK were taken to market by US companies, e.g. Campath for leukaemia and multiple sclerosis was marketed by Genzyme.

Scale and specialisation also have made it difficult for the UK to catch up. The US's larger venture capital are more likely to include specialist investors who will support sector-specific expertise and early stage biotech companies. In Europe, funds are smaller and less likely to invest in expertise per se. Larger funds also invest more in each investment round, on average. That, in turn, gives a company more flexibility in making choices and taking calculated risks.

The UK has had no such virtuous cycle, no breakthrough biotech drug successes. Instead, clinical stage failures have hit even the best funded firms in the UK, discouraging our primarily generalist investors. As clinical failures scared off investors, the sector shrivelled in the 2000s and the scars have been lasting.

Ironically, the UK biotech sector shrank in part in the 2000s not because of its failures, but because of its promise. Table 2 shows some of the major acquisitions of leading UK companies during that time. Although two were purchased by a UK firm, AstraZeneca, they still disappeared as separate innovative companies, depleting the sector.

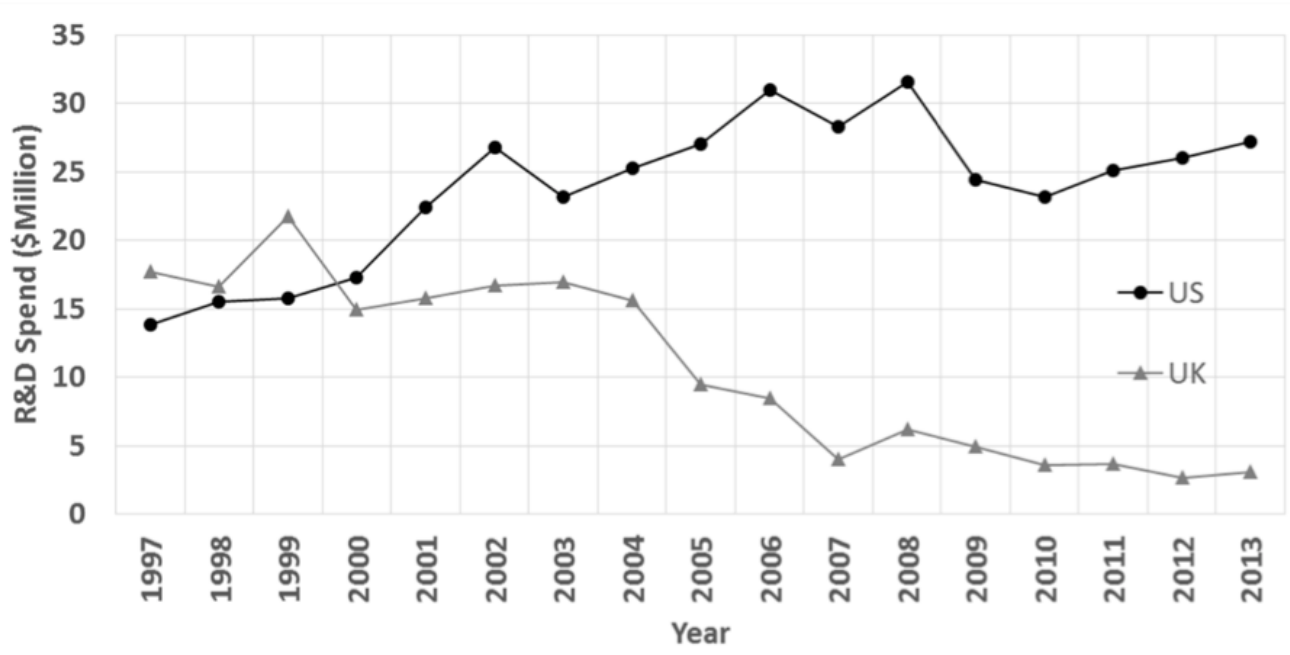
Table 2. Acquisitions of UK biotech leaders

Acquirer	Target	Deal value ($M)	Year
Chiron (US)	Powderject	810	2003
UCB (Belgium)	Celltech	2700	2004
AstraZeneca (UK)	KuDOS	210	2005
AstraZeneca (UK)	Cambridge Antibody Technology	1070	2006
Novartis (CH	Neutec	586	2006
GlaxoSmithKline (UK)	Domantis	454	2007
Sanofi (FR)	Acambis	550	2008

Note: This is a selective list

Figure 2 shows the median spending in the biotech sector in the US and the UK from 1997 through 2013. The excitement and nearly equal spending in the 1990s is evident here. But spending then declines in the UK for two reasons: first, some of the leading UK companies were bought up and disappear from the dataset and, second, investors are no longer willing to invest more money in the sector.

Figure 2. Median R&D Spend for UK and US therapeutic biotech firms (1997-2013)



Source: Authors' analysis based on data Nature Biotech annual survey, Public Biotech: the numbers, various years.

Taking a closer look at the companies in each country, Table 3 shows that the US has more of its companies in the higher market capitalisation categories and the UK companies are clustered in the two lowest categories. Only the US has firms with a market capitalisation of greater than $50 billion; none of the UK's companies are that large. This is not unexpected, for reasons we have discussed above. But what is important is that the US has a substantial number of firms in the middle tier.

Those companies are positioned to grow and fill in any space in the higher capitalisation categories the might be left when larger companies merge or are acquired.

Table 3. Size profile of firms in the US and UK therapeutic biotech sector: snapshot from 2013

Market Capitalisation ($)	0-49.99m	50m-499m	500m-4.99bn	5bn-49.99bn	>50bn	Total firms
All US (2013)	19.5% (38)	42.6% (83)	31.3% (61)	4.6% (9)	2.1% (4)	195
All UK (2013)	29.6% (8)	59.3% (16)	7.4% (2)	3.7% (1)	0	27
US Post-97s (2013)	20.8% (31)	46.3% (69)	30.2% (45)	2.7% (4)	0	149

Source: Adapted from Owens and Hopkins, 2016, p. 190.

9. Could the Government Have Done More in the UK to Encourage the Biotech Industry?

We doubt that greater public investment earlier on could have made a substantial difference because the ecosystem was underdeveloped. The effect of greater investment might only have been to build more companies that were bought earlier.

After the founding of Celltech in 1980, both Labour and Conservative UK governments avoided sector-specific policies and focused on a horizontal policy framework that supported enterprise in general—encouraging venture capital, university spin-offs, technology transfer, etc. (Lacasa, Reiss and Senker, 2004). In 2009, events conspired to again attract government attention. These included the report by the UK's Bioscience Innovation and Growth Team that focused on the biotech sector, Pfizer's 2011 decision to close its research laboratory in Sandwich, and concerns about other large pharmaceutical companies potentially de-emphasizing research in the UK. This led, for example, to the establishment of the Office for Life Sciences in 2009 and a ministerial appointment that focused specifically on the sector. The Biomedical Catalyst Fund was launched by the Coalition government in 2012 and run jointly by the Medical Research Council and the Technology Strategy Board. Most recently, in late 2017, a proposed comprehensive, forward-looking life sciences strategy (Bell, 2017) was detailed and the anticipated "sector deal" was announced (Department of Business, Energy & Industrial Strategy, 2017). All these initiatives are similar to policy instruments that the US has had for quite some time.

Over time, new limitations have been placed on the scope of industrial strategy interventions, primarily as a result of international commitments. The World Trade Organisation (WTO) was not in operation when the UK's highly successful pharmaceutical industry was developed just after World War II, nor was the UK a member of the European Union (EU) which imposes limits on state assistance that preclude investments of more than just a few million pounds in individual companies. Brexit will not necessarily solve those issues because the UK will remain in the WTO. A recent example of WTO constraints is the case of Bombardier, a Canadian aerospace and transportation company. The US has threatened WTO sanctions on its products, claiming the company has received excessive investment from the Canadian government. The UK's external trade commitments, made to benefit the country as a whole, then, still could limit government investment in individual life sciences companies.

Perhaps more could have been done to stimulate domestic biotech by procuring products from UK companies for use in the National Health Service (NHS); but this might have required the UK's civil service to appear to favour one company over another, something it has been hesitant to do. The effect might have been insignificant anyhow. Although 40 years ago the UK NHS was an important revenue source that made developing drugs in the UK attractive, that has changed as controls on NHS spending in medicines has increasingly tightened. The UK health care market is a shrinking proportion of the international market, partly as a result of these tighter restrictions, but also because markets abroad have expanded, e.g. in middle-income countries.

10. Can the UK's Disadvantages be Overcome?

Even if no limitations on UK actions existed, some of the US advantages would be difficult to imitate.

1. As noted above, the effects of scale are important: specialist, large and liquid capital markets support US biotech firms. In practice, this means that US firms are capitalised more highly and have more to spend on research and development (R&D).

2. Perhaps in part because of scale, US biotech benefits from complementary cross-sector effects. The large and successful venture capital sector supports several technology sectors, which themselves interact: the science base in both the public and private sectors, electronics and IT, established pharmaceutical companies, and biotech firms of all sizes. Often, these resources are co-located in major clusters. The knock-on effect of success in one sector on success in another continues to be important in the US.

3. The US has developed an "industrial commons" in biotech as early success led to a virtuous cycle of investment, talent recycling and more success. Certain areas have built up a depth of resource and expertise over the decades that would be difficult to replicate. For example, for a company planning to set up biomanufacturing, the Boston area has accumulated the needed expertise—in all the required areas—thus making it more attractive than nearly anywhere in the UK, where such resource centres have not developed.

4. The EU is large enough to develop important institutions that can foster the interstate collaboration that approximates the scale in the US, e.g. harmonisation of regulations under the European Medicines Agency (EMA) and patents under the European Patent Office (EPO). The EU R&D programmes also can play a facilitative role. But European health care markets remain fragmented, with different rules for drug pricing and reimbursement. The US still is the market of choice. Products may be introduced later, or not at all, in individual EU markets that provide serious price barriers and other disadvantages.

What the UK still seems to be yearning for is a flagship success, or series of successes, that will inspire investors to consider the UK biotech sector as a profitable place to invest. The UK at present, however, does not currently have either the critical mass or the right mix of firms to achieve this. It has too few companies in the crucial mid-size market capitalisation category. The UK sector is still dependent on AstraZeneca and GSK. Should either be bought out or merge, few companies are ready to replace them; those that are may themselves be sold, an eventuality that government cannot prevent. In the US, if we look beyond the Gileads and the Celgenes, we see a large tier of companies with considerably larger market capitalisations than most of their peers in the UK.

With that in mind, the 2017 Life Sciences Strategy is quite optimistic in its goal to "create four UK companies valued at >£20 billion market cap in the next 10 years" (Bell, 2017, p. 7), given that we have only produced one of those companies in the past 40 years — Shire, which moved to Ireland for tax reasons. The tools government has at hand for creating those firms and ensuring they remain separate entities are probably not sufficient. But what government certainly can do is invest in the science base to increase its size and diversity, which in turn will supply the talent to lead and staff emerging biotech companies. Currently, the UK has a smaller proportion of its gross domestic product (GDP) invested in this science base than do many European countries, the US and parts of Asia.

The biotech industry in the UK would benefit from smoother technology transfer arrangements and an enhanced role for the NHS as a supporter of drug innovation. Some are concerned that this would only place a greater burden on an NHS that now is struggling just to provide basic services. The cost may seem greater than the benefit.

11. Brexit and Beyond

Brexit may make some of the challenges identified above more difficult to meet. Funding, and collaboration, through research grants may be threatened. Academics already are making difficult choices about whether their next research proposal should be tailored towards winning a UK Medical Research Council grant or a European Research Council grant. Some are not applying for EU grants because they believe that applications from the UK will not be as favourably received as they might have been before the Brexit vote. In terms of funding, around 14 percent of UK research income is from European funding sources, and it is difficult to imagine UK sources being able to make up the shortfall. Just as serious is the potential dampening of access to collaborative networks, e.g. through the Innovative Medicines Institute (IMI) and the likely re-imposition of barriers to freely working, or studying, anywhere within the EU. Brexit, then, may impose some important limitations to strengthening and maintain the science base.

Brexit is likely to have an as-yet undetermined impact on supply chains. Not being part of the EU may make moving materials in and out of the UK more time-consuming and potentially more expensive. It is possible that this will mean that companies look less favourably at the UK for inward investment, for setting up new facilities and even maintaining current facilities here. A similar concern is that the UK may lose its reputation as a desirable place to base a European life sciences business; if Brexit distances the UK from European markets and institutions such as the EMA, then the attractiveness of the UK as a base in Europe diminishes.

The UK medicines market will without question be affected by Brexit as the UK will no longer be part of the EMA. We will need to re-establish our own regulatory system, which will be expensive, time-consuming and delicate. Unless our regulatory requirements coincide closely with those of the EMA and with the harmonised EMA-FDA requirements, companies may be less than enthusiastic about preparing a separate dossier for the relatively small UK market. This could delay, or preclude, marketing some new drugs here and it also would mean that UK companies might face additional expense if they wish to market in both the domestic market and markets abroad.

The UK has substantial venture capital funding compared to the rest of Europe. Some of that venture capital comes through the European Investment Bank, which potentially could be affected by Brexit. It is unclear, however, whether this will substantially affect non-EU international capital flows.

Initially, the reaction within the life sciences sector to Brexit was dark — shock, worry and deep gloom. A gradual shift has happened, and a more balanced assessment is emerging about what Brexit might mean and how departure from the EU could be turned to the UK's advantage. The report by Bell is interesting in that context. He suggests this is an opportunity: "If managed carefully, EU exit may be used as a catalyst to take steps to speed the growth of the life sciences sector in the UK" (Bell, 2017, p. 13). The approach recommended in the report provides a glimpse into a potential post-Brexit biotech world.

With respect to financing, Brexit will remove EU constraints on state aid to industry and may allow the UK government to be more generous with its support to the biotech industry. Arguments continue about whether that is desirable in itself, but Bell does seem to envisage a greater role for government, along with other funders. This includes financing not just early stage research, but also "large research infrastructure projects and high risk 'moonshot programmes', that will help create entirely new industries in healthcare" (Bell, 2017, p. 19). This would take the form of what he calls the Health Advanced Research Programme (HARP), which appears to be modelled on the US's Defense Advanced Research Projects Agency (DARPA, 2017). Bell views HARP as indispensable to the out-of-the-box thinking that he sees as essential to creating new biotech sectors in, for example, the application of genomics. This suggestion has generated much discussion in the UK about whether DARPA is an appropriate approach here. Perhaps the more relevant question is whether the government can afford to support HARP in the way Bell is suggesting at the same time it is expanding the newly-formed UK Research and Innovation organisation due to launch in April 2018 (UK Research and Innovation, 2017).

An important issue without a definitive answer is why UK biotechs disappear too early, before they have reached maturity, often through acquisition by foreign companies. Bell uses Cambridge Antibody Technology and as an example where sufficient capital for scale up could have kept it independent. Funding, Bell argues, need not necessarily be market capital; in continental Europe several life sciences companies are owned or controlled by families or foundations, making them virtually invulnerable to being taken over. He also points to the US example where new high-tech companies have created dual share classes that allow the founders to effectively control the company, which can help preserve independence. As we noted above, however, such short-termism has been a far less important brake on the growth of biotech in the UK than the lack of major successes which, had they occurred, would have encouraged more investment from a wider range of sources.

Foreign takeovers need not be viewed as wholly undesirable. Inward investment in the UK biotech sector, whether in the form of new factories or new laboratories or acquisitions, has been good for the sector. Recent Japanese acquisitions, for example, have been made specifically because the acquirer sees the UK as a source of high quality science and research, and intends to continue investing in the UK firm that they have bought. Solexa provides another excellent example of why using UK ownership as a criterion for the success of biotech firms in the UK can be misleading. Solexa was a Cambridge-based sequencing company regarded as a leader in that area; it was bought by US-based Illumina. Solexa R&D in and near Cambridge has continued to flourish, which supports the idea that ultimate ownership may be less important than what goes on in the UK.

Those who propose that the present government take a somewhat more protectionist stance on foreign investment have perhaps a too narrow view of the biotech industry. Bell, for example, suggests that in return for NHS involvement in R&D, the government "in some cases" would hold

a "'golden share' … to ensure that the company would continue to be based in the UK and would provide ongoing benefits to the health system" (Bell, 2017, p. 16). Although the idea is innovative, and such use of the NHS certainly is possible, the "golden share" idea seems to fail to appreciate the global nature of the biotech industry — and perhaps also the unintended negative repercussions that protectionism entails. Biotech is, and will only increasingly be, a global sector. It is vitally important post-Brexit that the UK does everything possible to maintain and seek to enhance our global and European connections, and that goal should figure centrally in the government's industrial strategy.

Finally, perhaps more thought and discussion needs to be directed toward how best to measure the success of the British biotech sector. Using the number and market capitalisation of independent biotech firms can substantially underestimate the success of British biotech. What matters more are the discoveries — whether they are made in universities or small biotechs or companies with the highest market capitalisations. Even Genentech and Genzyme were acquired.

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Office of Health Economics Research

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OHE is a charity (registration number 1170829)
Office of Health Economics, 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT
Tel: +44 (0)20 7747 8850 • **Fax:** +44 (0)20 7747 8851 • **Web:** www.ohe.org
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