Imperial College London

Sectoral Systems of Innovation and the UK's Competitiveness:

The UK Biopharmaceutical Sector

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Executive Summary

The UK has a globally strong reputation in the life sciences and a large pharmaceutical and biotechnology industry. This report investigates the current structure and performance of UK biopharma, which we define here as companies involved in developing and manufacturing both traditional pharmaceuticals and biotechnology-based pharmaceuticals.

We investigated trends in the economic performance of these companies and compared them to other leading countries, along with their research and development (R&D) capabilities and activity.

The biopharma ecosystem is one of the UK's leading industrial sectors, responsible for almost 400,000 jobs and an annual turnover of about £150 billion. It contributes a gross value added (GVA) of around £15 billion annually to the UK economy.

The sector's economic performance compared to competitor countries over the last 15 years has been poor.

Biopharma GVA has failed to grow in real terms since 2008 and the UK has fallen behind other competitor countries in international rankings.

The UK has seen a consistent downward trend in biopharma labour productivity and has been overtaken by other European countries.

Exports of pharmaceutical products have been in continuous decline since 2015 and the UK's net trade balance fell from around £6 billion to a negative balance of just under £1 billion between 2010 and 2020.

Medicines manufacturing volume has fallen by 29% and 7,000 jobs have been lost since 2009, partly as manufacturing of lower value generic drugs and active pharmaceutical ingredients has transferred to lower cost locations.

We identified strengths in biopharma R&D, with a total annual investment of £15 billion by the UK's two leading pharma companies (GSK and AstraZeneca) and a large number of small biopharma companies that are R&D active. There is also high inward investment by companies conducting R&D in the UK.

The UK ranks fourth in total biopharma R&D spending and third for R&D activity when measured by the location of inventors of patentable innovations.

The R&D output of UK companies tends to be at an early stage and there are concerns that the decline in clinical trial infrastructure in recent years is hampering R&D and launches of new drugs in the UK. Moreover, small companies find it hard to obtain private capital investment to move innovations through the development pipeline, and there is concern that too many companies are bought by non-UK players before they grow in size.

We believe there are opportunities to foster R&D productivity, scale-up small and young companies, and gain a competitive advantage in manufacturing high-value medicinal products, such as advanced therapeutics. There are also opportunities in new areas where data science is transforming the drug development process and where the UK has strengths in AI technologies.

Government and industry are making efforts to address some of the current challenges faced by UK biopharma, especially around the clinical trials infrastructure. However, we believe there is a need for a more integrated national life sciences R&D ecosystem that provides an agreed vision and targeted support for drug discovery, early clinical development, and adoption into the healthcare system.

Our main recommendations to stimulate R&D productivity and the overall economic performance of the UK's biopharma sector focus on improvements to the business environment (including targeted support for biopharma companies in the early and scale-up stages), clinical trials capacity building through enhancements to the data infrastructure, monitoring the performance of the new NHS integrated care systems in promoting and adopting innovations, strengthening the biopharma manufacturing base, and establishing a long-term sustained vision for pricing and market access for innovative drugs that is shared by all stakeholders.

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Section 1: Sector background

The UK has a strong and longstanding reputation for the life sciences. It has world-leading universities, with researchers generating the largest number of papers after the USA and China, resulting in a very high weighted volume of citations. It has been ranked second globally in attracting foreign investment in life sciences. [1] The pharmaceutical sector is one of the UK's leading industrial sectors, responsible for almost 400,000 jobs and contributing a gross value added of around £15 billion to the economy each year (see section 3). The UK is home to two of the world's largest pharmaceutical companies – GSK and AstraZeneca – and numerous smaller companies active in R&D.

We focus in this report on drugs based on chemistry (small molecule) and biotechnology (large molecule) production processes, and its industrial sector. For convenience, we describe the sector as 'biopharma'.

The UK aspires to be a world leader for the development, commercialisation and adoption of new and innovative biopharma products, yet there are concerns about the UK's ability to sustain the sector's global competitiveness over the longer-term. The sector is experiencing pressures across its full range of activities, ranging from the R&D phases in drug development to commercialization and adoption. Some of these pressures are global. Biopharmaceutical companies around the world are experiencing pressures associated with the scientific challenges of drug discovery targeting more complex diseases. Other challenges relate to the lack of economic incentives to develop drugs for rare diseases, antibiotic resistance or new vaccines. Companies are also facing increased environmental and safety regulation, and stricter controls by governments and purchasers on prices paid for drugs.

BOX 1. DEFINING 'DRUGS'.

Pharmaceuticals are substances used as medicinal drugs to prevent, treat, or alleviate symptoms of diseases or medical conditions. They usually comprise small molecules designed to have specific pharmacological effects and are typically synthesized through chemical reactions or extracted from non-living natural sources. They are commonly available in various forms, including tablets, injectables, creams and liquids.

Biopharmaceuticals, or 'biologics', are therapeutic agents derived from living systems, such as microorganisms, plant cells, or animal cells. They are manufactured using biotechnology processes, including use of fermentation and cell culture in bioreactors to generate the desired proteins and further purification steps to ensure quality and safety. Biopharmaceuticals offer targeted and personalized treatments due to their high specificity and effectiveness.

But other challenges are more homegrown. There has been a drop in clinical trials conducted in the NHS, prompting concerns about the attractiveness of the UK for launching new drugs. The slow adoption of proven products and the barriers that hinder the timely spread of new healthcare technologies has long been highlighted in the UK, which lags behind other European countries in access to newly-approved medicines (see section 3). And despite the strong research base, the sector is dominated by small and medium-sized enterprises (SMEs) that rely on successive fundraising rounds to maintain cash flow and are frequently acquired by companies from the USA or elsewhere without growing into large UK companies. [2] There are also concerns about the UK's challenges in competing with other countries in the manufacturing stages of drug development – manufacturing capacity has been lost to other countries, both through outsourcing and the growth of manufacturing of generic drugs elsewhere, impacting on imports, self-sufficiency and jobs. [3,4]

The nature of biopharma as an industrial sector is also slowly evolving, driven by innovation in the technologies underpinning drug development and creating niches for the entry of new players. The nature of drug discovery and development is beginning to change through the application of data science, including artificial intelligence (AI), the availability of comprehensive drug and chemical databases, and advances in computational life sciences and engineering biology (the application of engineering principles to the design of biological systems). These technologies offer the prospect of faster drug development and better targeted products, for example by enabling rapid screening of data to generate potential leads or cheaper drug trials.

This evolution in drug development technologies has been accompanied by emerging ecosystems which bring together new specialist players and the 'traditional' large pharmaceutical companies. These include a drug repurposing ecosystem and an innovation ecosystem based around engineering biology. [5] The former comprises specialists providing data science and database technologies and platforms, university or other research centres, small start-ups developing repurposed drugs using open-source data or working with larger biopharma companies, and non-profit funders and patient-led groups focused on cures for rare diseases. The engineering biology ecosystem links specialists in data science, biology, genetic manipulation, fermentation, chemistry and robotics.

These emerging ecosystems are dynamic, involving a variety of interdependent organisations, playing different roles in the innovation process, and begin to raise questions about how to define the 'drug industry' or a 'drug company'. The processes and organisations involved in developing drugs are increasingly varied, involving a wide range of routes and players. New companies are emerging which provide competences not possessed by traditional large drug companies, but they may also disrupt the traditional pharmaceutical companies. Although the level of appropriability in biopharma is high – protection of intellectual property is strong – the underpinning technologies and knowledge and skill sets are relatively generic, making incumbent firms potentially vulnerable to innovative new players. [6]

The importance of bringing the new players and communities together and building understanding between them has not gone unnoticed. [5,7,8] The strength of these biopharma ecosystems are pre-requisites for a globally productive UK pharmaceutical sector. Ensuring the sector is able to raise its 'innovation productivity' – the ability to develop and commercialise new products faster and more affordably – will be essential if the UK biopharma sector is to remain globally competitive and meet the demand for affordable drugs.

The UK has a strong life science base with good public funding and the NHS provides a single anchor customer for its products. This context offers good opportunities to build on the existing strengths of UK biopharma. Over the last decade, there have been numerous reports from government and industry bodies which identify areas and prescriptions for improvement. But the problem is not diagnosis or lack of ideas – the problem is an 'execution gap' in momentum and support for key initiatives, according to Emma Walmsley, head of GSK. [9]

This study presents findings from a review of the key technology, business and policy trends which will influence the future productivity and competitivess of the UK's biopharma sector. We draw lessons for policymakers seeking to maximise the UK's potential in this field.

The next section of the report describes the broad context within which the UK biopharma sector is operating, including global and national trends. We then discuss the findings from our analysis of key indicators of the health of the sector. In the final section we outline our conclusions and recommendations for policymakers and business.

BOX 2. RESEARCH METHODOLOGY

The appendix provides details of data sources and methods to analyse it. To characterise the UK's biopharma sector, we created a firm-level database by combining two datasets, from the 2019 'Biopharma core' dataset provided by the Office for Life Sciences and the GMDP database by the Medicines and Healthcare Products Regulatory Agency (MHRA).

We extracted firm-level financial and economic variables from data provided by Bureau van Dijk and used Pitchbook to extract data on international private capital investments in biotechnology and pharmaceuticals.

Other sources of data include the NIHR Innovation Observatory Scan Medicine database and the EU R&D Investment Scoreboard.

Section 2: UK Performance and International Comparison

This section describes the background context for the UK's biopharma sector – the forces shaping the activities of the sector and its component parts. Some of these forces result from technological innovation, others from social or economic trends, or policy decisions.

The global context

The R&D 'productivity crisis' in drug development

The challenges faced by the pharmaceutical industry in developing new drugs are long-standing and well-known. This is not a uniquely UK problem – drug companies around the world are facing similar pressures from a decline in R&D productivity. This has been highlighted by industry leaders, observers and researchers, and policy makers since the late 1990s, although most recent investigations have shown a slight upward trend in terms of number of new drugs per R&D spending (see box 3).

The reasons for this have been widely investigated and there is some disagreement about the relative impact of different factors. These include increased attrition (failure) rates across all drug development phases, investment in therapeutic areas associated with high risk of failure [15], and tighter regulations.

It is important to note that the measures commonly used in discussions on R&D productivity have limitations. In particular, simply focusing on the number of new drugs does not measure or adjust for their value for scientific progress, patients, and society. Some commentarors suggest that the real innovation crisis lies in the decrease in the number of drugs that offer true therapeutic advances. [16,17]

As well as the long-term fall in R&D productivity, drug companies have had to confront a series of other challenges which have impacted on the profitability of drug development:

- Regulatory costs have increased due to the need to generate more demanding and higher-quality clinical data.
- There is downward pressure on prices, with much greater focus by regulatory bodies and payers (e.g. insurance companies) on the societal benefits and economical costs of drugs.
- The use of lower-cost generics and biosimilars has grown; European and US drug companies face more competition from generic manufacturers based in India and elsewhere, and there is more rapid 'genericisation' after a branded drug's patent expiration. [20,21]

BOX 3. THE LONG-TERM DECLINE IN R&D PRODUCTIVITY

Measured by new drugs authorised by the Food and Drug Administration (FDA) each year, there was steady growth from the mid-1960s to the mid-1990s. Since then, the number has consistently declined. At the same time, the total cost of R&D steadily rose, resulting in a significant decline in R&D efficiency. [10–13] The number of new approved drugs per billion US dollars, adjusted for inflation, fell from around 50 per year in the 1950s to under one drug per year by the 2010s, with the first wave of biotechnology derived therapies in the 1990s having no effect on the decline in productivity. [14]

The most recent investigations into R&D productivity / efficacy have shown a slight upward trend in terms of number of new drugs per R&D spending. This seems to be associated with a decrease in attrition rates at all drug development stages. While research has found that significant R&D investment into highly specialised therapeutic areas (e.g. rare diseases) is associated with higher risk of failure, validation of drug targets has been improving through the application of data science technologies (e.g. genome-wide association studies), and the time to terminate failing R&D projects has decreased. [18,19]

Changing drug development technologies and ecosystems

The rising cost of developing new drugs, coupled with increasingly stringent value for money expectations of governments and regulators, led pharmaceutical companies to restructure and seek new R&D and business models. An initial strategy for companies facing expiring patents and a lack of new drugs in their pipeline was to embark on mergers and acquisitions. [22–24] The effectiveness on R&D productivity remains inconclusive. [20] Pharmaceutical companies also reformed their internal innovation processes to make faster decisions about terminating R&D projects and outsourced or out-licensed projects. In time, a consensus emerged that drug discovery and development is often better accomplished

through collaborative R&D (such as 'open innovation'), alliances between biotech and pharmaceutical companies around specific therapeutic areas, and collaborations with specialist firms providing data science tools and platforms. The relationship between biotechnology and pharmaceutical sectors has evolved over time. Partnerships provide funding and access to new product opportunities for both sectors. Advances in biotechnology, including recombinant technology and genetics, have introduced a more systematic approach to drug development overall (see box 4).

Drug development therefore takes place in an increasingly complex and segmented way. Several different R&D models have been adopted. Some companies focus on developing new drugs in-house or through licensing. Others pursue a similar strategy but also engage in generics. Large diversified companies invest across multiple areas. Some generic drug companies have diversifed from generics into drug development. Some pharmaceutical service companies are expanding their own innovative activities.

Data availability and data technology, especially AI, are beginning to play a pivotal role in transforming the early-stage drug development process by identifying and validating new drugs and their targets more efficiently. [26] A new ecosystem is beginning to emerge, driven by a proliferation of startups with occupying specific niches in biopharma R&D and creating new nichers (see box 5). As yet there is no consensus on the overall impact of these strategies on R&D productivity, but the adoption of AI technology and the availability of comprehensive drug and chemical databases, coupled with rapid advances in the experimental and computational life sciences, does appear to be removing some of the serendipity from drug development. [27,28]

BOX 5. THE NEW DRUG DEVELOPMENT ECOSYSTEM

There were an estimated 600 active AI-driven companies involved in biopharma in at the end of 2022, including approximately 50 based in the UK. Investment increased from $2.28bn to $2.93bn between 2020 and 2021. [29] The overall global market for drug discovery technologies has recently been estimated at $55bn per annum and is expected to grow to $157bn by 2030. [30] One challenge for the sector is the global shortage of data science expertise, with most AI specialists being acquired by tech corporations instead of pharmaceutical companies. Another challenge is the lack of accessible high quality data for deep learning technologies due to privacy, ethical, legal, data ownership, and regulatory issues.

A specialist subsector, with its own emerging ecosystem is drug repurposing (identifying potential new uses for existing drugs). [31] At least 65 companies and other types of organisation such as rare disease NGOs, offer drug repurposing services to the pharmaceutical industry, in a market currently valued at $313 million. This is projected to to be worth over $1.2 billion by 2030. [32]

BOX 4. THE CHANGING DRUG DISCOVERY LANDSCAPE

The drug discovery landscape has undergone considerable change over the past decade, driven by the integration of new technologies into drug development processes. [25] Traditional pharmaceutical companies have increasingly outsourced the early stages of scientific research to organisations and companies with specialist expertise, such as in genomics and proteomics, and are increasingly collaborating with data science companies. A more diverse range of players are now actively engaged in collaborative arrangements to identify new drug candidates, conduct preclinical research on cell-based and animal models, and design and manage human clinical trials. Collaborations with contract research organizations (CROs), specialist technology platforms and academic institutions have enabled traditional pharmaceutical companies to expand their drug discovery capabilities and gain access new areas expertise and technologies. Outsourcing operations to CROs and contract development and manufacturing organizations (CDMOs) helps pharmaceutical companies reduce costs and improve efficiency by providing flexible capacity to accommodate changes in demand for the production of drugs.

Digital transformation in the pharmaceutical industry

Beyond drug discovery, pharmaceutical companies are seeking to embrace a digital transformation of their activities to move from traditional product-centric operations to more patient-centric and service-oriented business models. It is suggested that the COVID-19 pandemic accelerated digital transformation by six years. [33] This is taking place across pharma value chains. Data-driven approaches are improving patient enrolment in clinical trials by better matching patients with studies. The integration of AI, robotics, and the 'internet of things' (IoT) can optimise real-time production of drugs within smart factories, driving significant cost savings and reducing errors and wastage. [34–36]

Digital transformation, as well as innovation in drug discovery technologies, may be blurring the boundaries between the pharmaceutical and medical device industries, with digital medicine innovations such as drug-device combinations. An example is the digital pill, which combines traditional medication with an ingestible monitoring sensor. [37] This raises questions about how to define a 'drug'. And the proliferation of different types of organisation involved in the drug development, especially from data science, makes the definition of a 'drug company' harder. It has long been argued that 'traditional' pharmceutical companies need to move 'beyond the pill' and find ways to marry existing business models with new value-adding revenue streams, either directly evolving from their existing products or focused on adjacent services and complementary products, or brand new healthcare related services. [38]

The UK context

Commercial environment

Since 1957, the Department of Health and the pharmaceutical industry have negotiated voluntary agreements covering pricing of branded medicines, designed to keep NHS drug costs under control while also encouraging investment in new drugs. The latest deal, signed in 2019, involved companies paying back 5 to 10% of UK sales if the NHS drugs bill rises by more than 2% annually. In 2022 the rate rose to 15% and then 26.5% in 2023. Governments in Europe also employ methods such as clawbacks and price limitations to control drug spending, but UK's clawback rate is now significantly higher than other European countries, where 10% or lower is common. However, Germany increased the mandatory discount on drug sale prices to 12% for 2023, while France plans to reduce its drug budget by 13%. The USA is undergoing a major pricing reform, with the federal government gaining the power to negotiate prices for treatments funded by Medicare. [39]

The increase in the clawback rate has resulted in a backlash from pharmaceutical companies. The Association of the British Pharmaceutical Industry (ABPI) argues that the high tariff could lead to a loss of £5.7 billion in R&D investment over the next five years and a loss of over £50 billion in GDP foregone by 2058. [40] While large pharmaceutical companies have not claimed their patented drugs are unprofitable under the UK's voluntary agreement, about 40% of the drugs covered by the scheme are off-patent, and the generic manufacturing sector of the industry is pushing for its drugs to be excluded, given their prices are 70 to 90% lower than the original drugs. [40]

Recently, AbbVie and Eli Lilly have withdrawn from the pricing agreement with the NHS. [40] Eli Lilly has paused a potential investment in the UK and has said that Europe's spending cuts are detrimental to its ability to attract R&D, clinical trial and manufacturing investment. Bayer has criticised the generally 'innovation unfriendly' environment in Europe and is reducing its presence in the UK. GSK and AstraZeneca have opted to build new factories outside the UK. Drug companies are also contemplating withdrawing from an agreement with the French government. [39]

It has been suggested that the UK's strengths in R&D may not be sufficient to mitigate drug companies' concerns about pricing policies and the commercial environment in the UK and Europe. 39 The exclusion of UK-based academics from EU research programmes, coupled with pricing policies and the UK's generally declining share of the global pharmaceutical market, all reduce the attractiveness for R&D investment. The head of International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) recently stated that the industry's warnings should not be dismissed as 'pure rhetoric' and pointed out that 'Not only are there great scientists in the US ... but you also get a return on investment in a tough environment'. [39]

R&D tax credits

The decision to cut R&D tax credits for small and medium sized businesses, and boost the rate for larger companies, has been criticised. [41] While concerns have been raised about the cost and value for money of such tax credits, research has shown that they were successful in stimulating R&D spending and patent registrations, particularly among younger firms. However, biotech and other science-based start-ups may be less affected than other types of company, for whom the current threshold of 40% for R&D spending is too high. The government is currently considering a new merged tax credit scheme.

BOX 6. UK PERFORMANCE IN CLINICAL TRIALS

- The number of clinical trials initiated in the UK annually fell by approximately from 765 in 2017 to 525 in 2021, and fewer commercially funded trials are initiated in the UK compared to other similar countries, although 2021-22 saw a better performance.
- The UK's global share of clinical trial recruitment was 3% in 2020, a figure that has not varied much since 2012 – Spain's share grew from 2.6% to 4.2%. [43]
- The number of participants in commercial trials supported by National Institute of Health and Care Research (NIHR) declined significantly from over 50,000 patients in 2017-2018 to just over 28,000 in 2021-2022. [42]
- Other countries have also seen a fall in trials, but the UK, Germany and Japan have experienced a sharper decline than other countries (see figure 1).

Clinical trial capabilities

The O'Shaughnessy report [42] found that the majority of the GVA arising from research supported by the National Institute for Health and Care Research (NIHR) clinical research networks (£1.8 billion) resulted from clinical trials funded by the life sciences industry. The return on investment includes direct health benefits, profits to UK firms involved in research, and spill-over effects on the wider economy.

In recent years, however, there have been weaknesses in the UK's performance in attracting clinical trials (see box 6), although this varies across different drug development phases – the decline is particularly pronounced in commercial phase 3 trials, where the UK has dropped from 4th to 10th in global rankings. [44]

This may have been partly exacerbated by a pivot towards COVID-19 research, which also impacted set-up and recruitment times, but international competition is also a significant factor. The UK is said to be perceived as an unreliable partner due to inconsistencies in approval processes and delays in site-level approvals.

The UK lags seventh behind the USA, Spain, Australia and other countries in time taken from regulatory approval to administration of the first dose to participants. The median time (247 days in 2020) saw an increase of 25 days since 2018, compared to Spain, with a median of 197 days (joint third). This leads to lower allocations from global pharmaceutical companies for patient recruitment in the UK. The O'Shaughnessy report found that other countries are seeking to attract trial activity. Denmark, for example, is actively encouraging collaboration between regulators, clinicians, companies and patients to ensure it is competitive in attracting clinical trials.

The government has responded by unveiling new measures address these concerns. [45] It has committed £121 million to reduce approval time to 60 days by addressing delays in the system, providing real-time data on clinical activity, establish a common approach to patient contact, and create clinical trial acceleration networks (CTANs). The goal is to quadruple the number of patients in clinical trials by 2027. Strengthening the clinical trials landscape is seen by the government as a way for the UK to regain its international position and expedite access to new treatments.

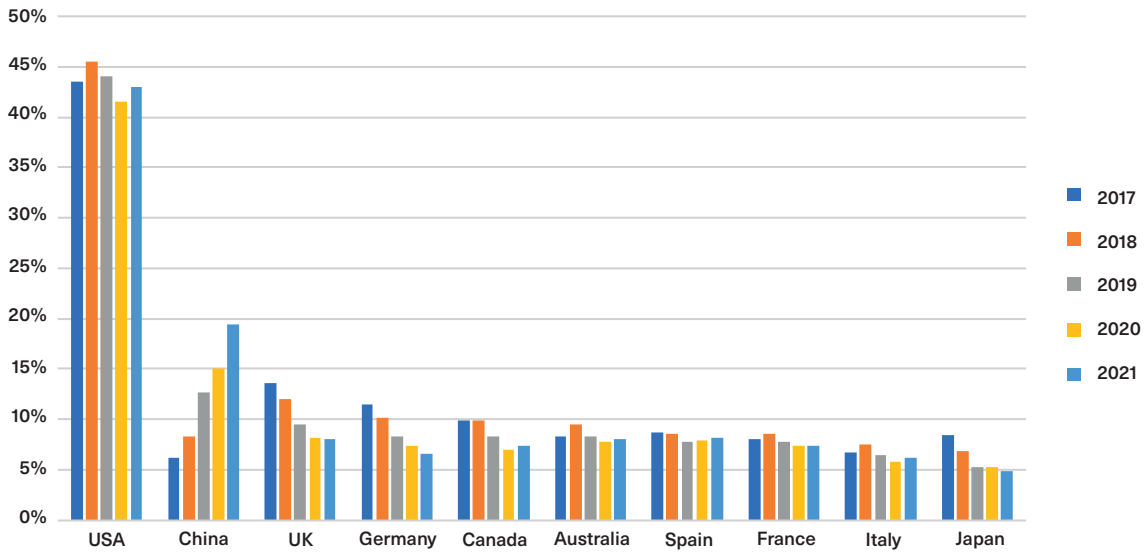

Figure 1: Proportion of initiated and completed clinical trials between 2017 and 2021 by trial site location. Source: NIHR Innovation Observatory Scan Medicine

Access to innovative drugs

There is concern that the UK is slower in adopting new drugs than comparator countries. Although the position has improved slightly in recent years, the UK lags behind other European countries even five years after launch of a new drug. England and Scotland ranked sixth and ninth in time taken for drugs to become available after market authorisation by the European Medicines Agency (EMA), with median times of 296 and 384 days respectively. [43] Over the long term, there has been a small (but not statistically significant) upward trend in the number of new drugs added to the British National Formulary that were not generics or new formulations (with periods of higher and lower activity). [46] Most drugs launched between 2001 and 2012 were categorised as only slightly innovative (in terms of therapeutic value), but with an upward trend. The number of highly innovative drugs launched annually remained relatively stable. [47]

While the speed of new drug launches in the UK – whether innovative or not – remains a concern, commentators have recently suggested that a bigger threat may be pharmaceutical companies withdrawing certain drugs from the UK and wider European market due to pricing concerns. [39] These reflect the increased scrutiny by regulators and health authorities over the value of drugs. Debate over the value of novel drugs and the mechanisms to cover their cost is likely to grow as the pharmaceutical industry focuses increasingly on expensive personalised and targeted therapies for rare diseases and specific mutations in oncology. Various alternative payment models, such as pay-for-performance or flat fees based on therapeutic requirements, are being explored and the Department of Health and Social Care has signed agreements to ensure they are accessible to the NHS.

Medicines authorisation

After Brexit in 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) replaced the EMA as the regulatory agency for drug authorisations. This has raised concerns that a separate application process would lead to additional costs for drug developers and delays in timely access to new drugs for UK patients, compounded by the UK's small share of the global pharmaceutical market. [48,49] The first study of the MHRA's regulatory activity post-Brexit looked at approvals in 2021, its first year of independence, compared to other international regulatory bodies. The MHRA lagged USA and EU in novel drug approvals and remained reliant on EU regulatory decision-making for approximately 70% of novel medicines approvals. There were significant regulatory delays for a small number of novel medicines in the UK. However, the MHRA has introduced initiatives which show early promise for faster authorization of innovative medicines for cancer and other areas of unmet need. [50] Partnerships with regulators in Australia, Canada, Singapore and Switzerland have also been introduced, and the government has announced that the MHRA can align with trusted regulators to save time and resources in authorising new drugs. [51]

BOX 7. TRENDS IN THE LOCATION OF BIOPHARMA MANUFACTURING

Only about 20-25% of the total number of generic drugs prescribed annually in the UK – which account for 81% of all prescribed drugs – are manufactured within the UK. Apart from the large growth in generic drug manufacturing in India, drug manufacturers have relocated production to the Republic of Ireland, supported by a combination of capital grants, low tax rates, and planning policies. [54]

The production of biologics has concentrated in the USA, Japan, Singapore, Switzerland and Ireland. [3]

The manufacturing base for active pharmaceutical ingredient (API) has transferred to lower cost locations, especially China and India, and questions have also been raised about the possible detrimental impact on the resilience of supply chains.[4]

Manufacturing

Manufacturing of drugs is important both to ensure resilience in the supply chains for key drugs and to support economic growth by creating high-value jobs in life sciences. Although the UK saw growth in pharmaceutical manufacturing employment between 2016 and 2019 [52], there remain concerns about the long-term loss of manufacturing activity to other countries, especially involving generic drugs.

Historically, the location of pharmaceutical R&D – where the UK has strengths – and commercial manufacture has tended to be closely linked. [4] However, since the early 2000s the manufacturing sector in the UK has been shaped by merger and acquisition activity and economic pressures. Falling sales margins, coupled with the cost of regulatory certification in older plants, have undermined their financial viability and led companies to close or mothball unprofitable manufacturing plants. As a result, there has been a rise in contract development and manufacturing operations (CDMOs), replacing direct manufacturing capability by larger pharmaceutical companies. [53] Manufacturing volume in the UK has fallen by 29% and 7,000 jobs have been lost since 2009 (see box 7).

Workforce

The biopharma industry is reliant on specialised skills, and there have been periodic reports of skill shortages in the UK. However, an ABPI survey of its member in 2022 indicated a decrease in skills shortages, suggesting that efforts to address the skills gap have had positive outcomes. [55] The number of priority fields displaying shortages has decreased over time, with only seven identified in 2022 compared to sixteen in 2018 and eighteen in 2015. Nevertheless, skill shortages were persistent in areas involving data science and modelling, as well as engineering in manufacturing.

Sectoral trends and international comparison

Contribution to the economy

The Office of National Statistics (ONS) reports annually on GVA for economic sectors, including the 'manufacture of basic pharmaceutical products and pharmaceutical preparations' (Standard Industrial Classification code 21). The data show that GVA for pharmaceutical manufacturing in the UK fell for the decade after the economic crash in 2008 and has recently seen an upward trend but has not yet fully recovered (Figure 2). Total GVA was slightly over £15 billion in 2020 (data after 2020 are not yet available).

The ONS data, using SIC code 21, exclude other sectors of the biopharma ecosystem, including companies that support the sector, perform R&D activities and biotechnology-based drug research. In a recent report, the ABPI used a wider definition, which estimates the GVA contribution of the entire UK life sciences sector was £36.9 billion in 2019. Of this, £16.9 billion were direct contributions by the economic performance of life sciences companies, while the rest represents indirect and induced contributions by supply chain and economic contributions by employees respectively. [8]

Figure 3 compares pharmaceutical GVA for different countries. The UK stands seventh and has fallen behind France and Italy over the last 15 years. The UK is also an outlier, with a downward trend in GVA, while Germany, France and Italy have been relatively stable over time. In contrast, the USA, Ireland and India have all demonstrates growth in GVA over time. These findings are in line with previous reports. [52,56]

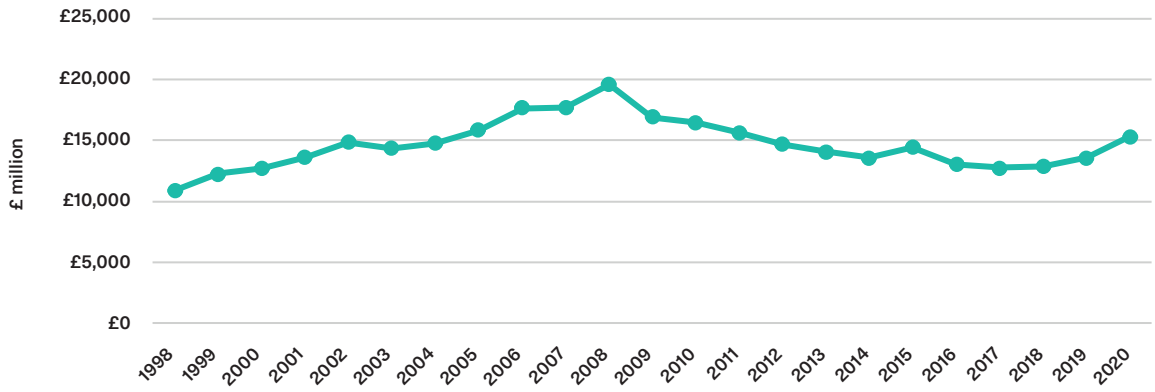

Figure 2 Regional balanced gross value added [GVA(B)] for UK economy for pharmaceutical manufacturing (SIC21) (chained volume measures, £ million, excludes effects of inflation). Source: Office for National Statistics

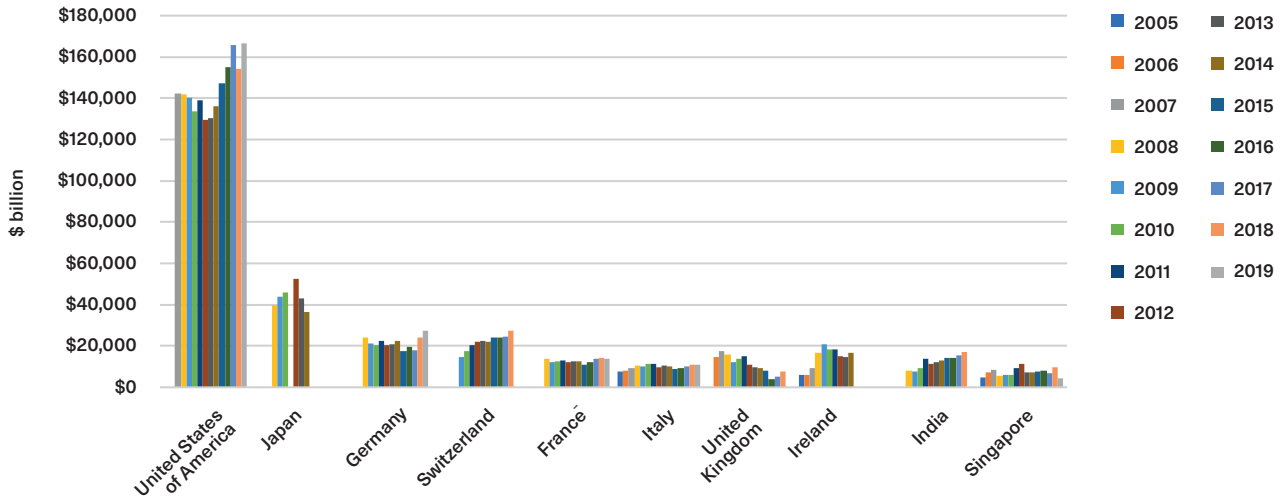

Figure 3: International comparison of GVA figures for pharmaceutical manufacturing. Displayed are the top 10 countries with the highest GVA figures over the observed time frame. Note: some data points are missing across countries and years. Source: Calculation by study authors by data from UNIDO INDSTAT 4 2022, ISIC Revision 4

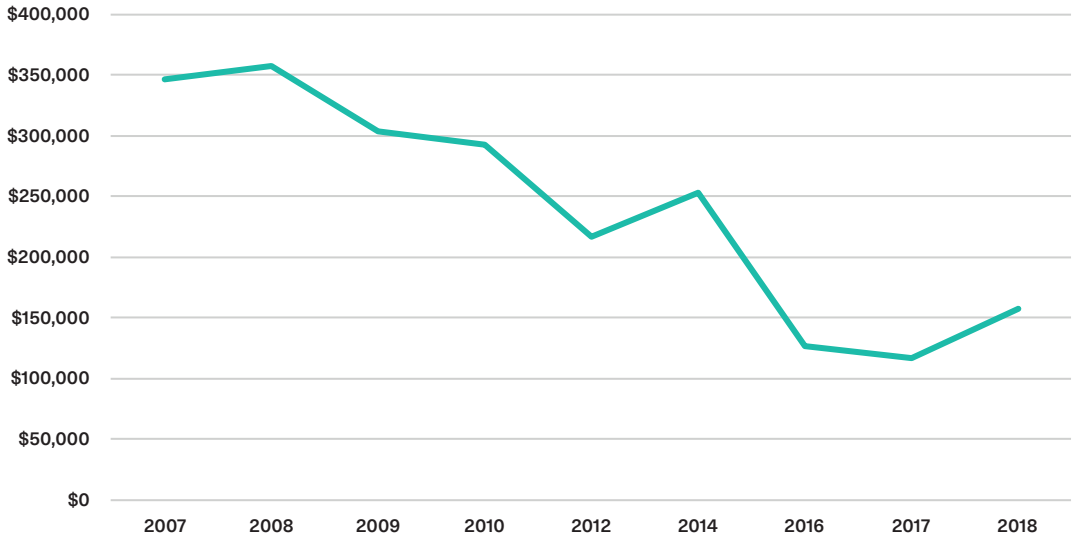

Figure 4: GVA per employee for manufacturing of pharmaceuticals in the UK. Source: Calculation by study authors by data from UNIDO INDSTAT 4 2022, ISIC Revision 4

Labour productivity

In the UK, financial and insurance activities (£145.1k), information and communication (£83.1k), manufacturing (£74.4k), and construction (£55.3k) had among the highest levels of labour productivity in 2019. [56] According to United Nations Industrial Development Organization (UNIDO) figures, GVA per employee for pharmaceutical manufacturing in the UK has continuously decreased since 2007 to £117.9k in 2018 (Figure 4). This is, however, still higher than the labour productivity of the UK manufacturing sector as a whole.

Singapore, Ireland, USA and Switzerland show the highest pharmaceutical industry labour productivity levels, characterised by periods of growth and stability since 2005. The UK has seen a consistent downward trend in labour productivity, and now ranks eleventh having been overtaken by other European countries (Belgium, Finland, Denmark) (Figure 5). These findings are in line with other reports showing falls in UK labour productivity of -9.5% between 2007 and 2017 [57] and -2% between 2015 and 2019 [8].

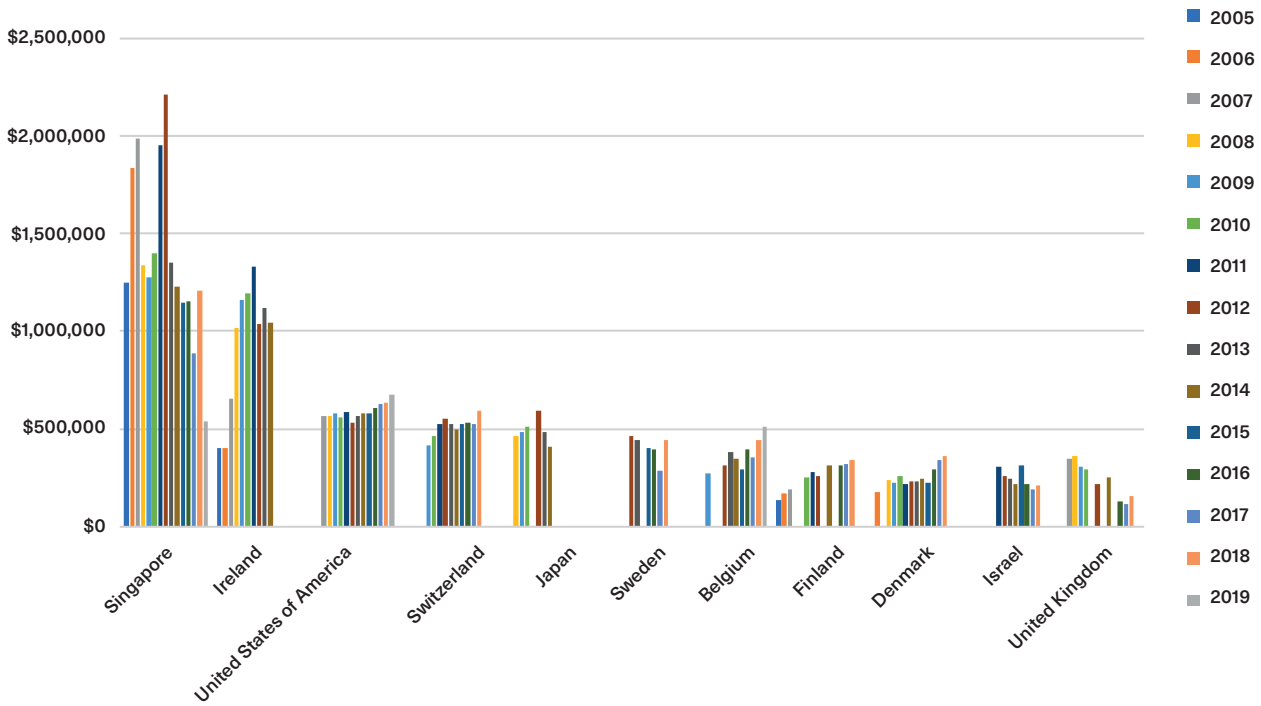

Figure 5: International comparison of GVA/employee figures for pharmaceutical manufacturing. Source: Calculation by study authors by data from UNIDO INDSTAT 4 2022, ISIC Revision 4

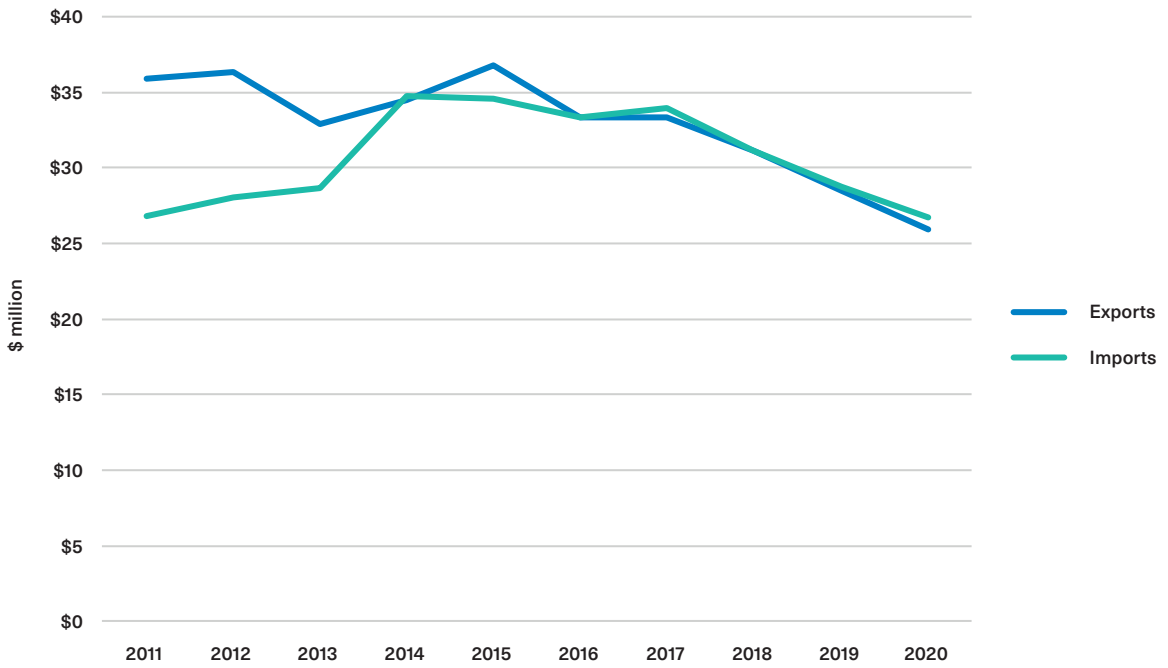

Figure 6: Export and import for pharmaceutical products for the UK. Source: Calculation by study authors by data from Life science sector data 2022 [52]

Trade balance

Imports and exports of pharmaceutical products have been in continuous decline since 2017 (Figure 6). This comes after positive trade balance figures between 2011 and 2015. Internationally, the UK's ranking has dropped 94 places since 2010, from fourth, with a positive trade balance of over £6 billion, to ninety-eighth, with a negative trade balance of slightly under £1 billion by 2020. The most consistent countries according to trade balance are Switzerland, Ireland, Germany, France, India and Israel (table 1).

2010		
Rank	**Country**	**US$bn**
1	Switzerland	27.9
2	Ireland	26.9
3	Germany	18.6
4	**United Kingdom**	**9.7**
5	France	8.5
6	Denmark	5.1
7	Israel	5.0
8	India	4.9
9	Belgium	4.8
10	Sweden	4.5
11	Singapore	3.4
162 of 162*	USA	-21.2

2020		
Rank	**Country**	**US$bn**
1	Ireland	27.9
2	Switzerland	26.9
3	Germany	18.6
4	India	9.7
5	Denmark	8.5
6	Netherlands	5.1
7	France	5.0
8	Belgium	4.9
9	Italy	4.8
10	Sweden	4.5
11	Singapore	3.4
98	**United Kingdom**	**-1.2**
133 of 133*	USA	-85.6

Table 1: International comparison of the trade balance for pharmaceutical products Source: UK Innovation Report 2022 [58]

R&D investment and environment

The UK's overall gross domestic expenditure on R&D (GERD) as a share of GDP was 2.93% in 2020. The methodology of GERD in the UK has recently changed, which led to an increase in UK GERD to a level that is now above the Organisation for Economic Co-operation and Development (OECD) average of 2.71%. [56] The government's R&D expenditure as a share of GDP was 0.12%, is below the OECD average (0.24%). [56] The ONS estimates total UK business expenditure on R&D (BERD) was £46.9 billion in 2021, an increase in £5.9 billion since 2018. Chemical and pharmaceuticals manufacturing was the third largest sector industrial sector, with R&D expenditures of £8.2 billion, accounting for 17.5% of total industrial R&D spending.

Public funding for life science R&D is reported and categorised by the UK Health Research Analysis (UK Clinical Research Collaboration), which reports £4 billion expenditure within the UK in 2018 (£2.5 billion direct spending and £1.4bn on infrastructure). There was also an additional £850 million in health-relevant funding from other sources (university and private not for profit). [59]

The EU R&D Investment Scoreboard is published annually and provides an annual list of the companies with the highest enterprise R&D spending worldwide (top 2500 companies) and in the EU (top 1000 companies). Across all industrial sectors, 95 of the world's 2,500 top R&D-investing companies have their headquarters in the UK, which ranks fifth behind the USA, China, Japan, and Germany. The top three R&D investing companies in the UK are the two pharmaceutical companies AstraZeneca and GSK and the bank HSBC. [56]

The Scoreboard data were used to benchmark the biopharma sector between 2014 and 2020, the timeframe with methodologically comparative data combining the EU and worldwide datasets. After 2020, the methodology excluded the UK from the EU list.

The UK consistently had the second highest number of companies amongst companies with the highest enterprise R&D spending worldwide, but China is closing the gap quickly (Figure 7). The UK scores fourth in total global R&D spending, behind USA, Switzerland, and Japan (Figure 8). However, when considering the average R&D spend by company, UK drops to ninth position behind countries including Switzerland, Germany, Israel, Japan, USA, France, and Ireland (data not shown). Most R&D by all pharmaceutical companies in the ranking is performed in the US and Germany, when measuring the location of patent inventors of patentable innovation. The UK is in third position for R&D activity (Figure 9).

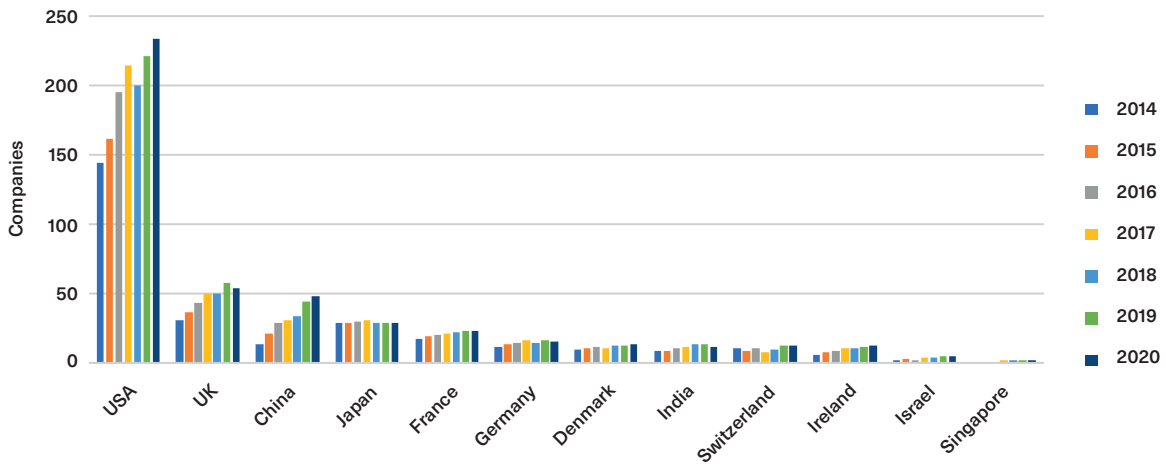

Figure 7: Number of companies by location of HQ amongst the companies with the highest enterprise R&D spending worldwide between 2014 and 2020. Source: Calculation by study authors by data from EU industrial R&D investment scoreboard 2014-2020

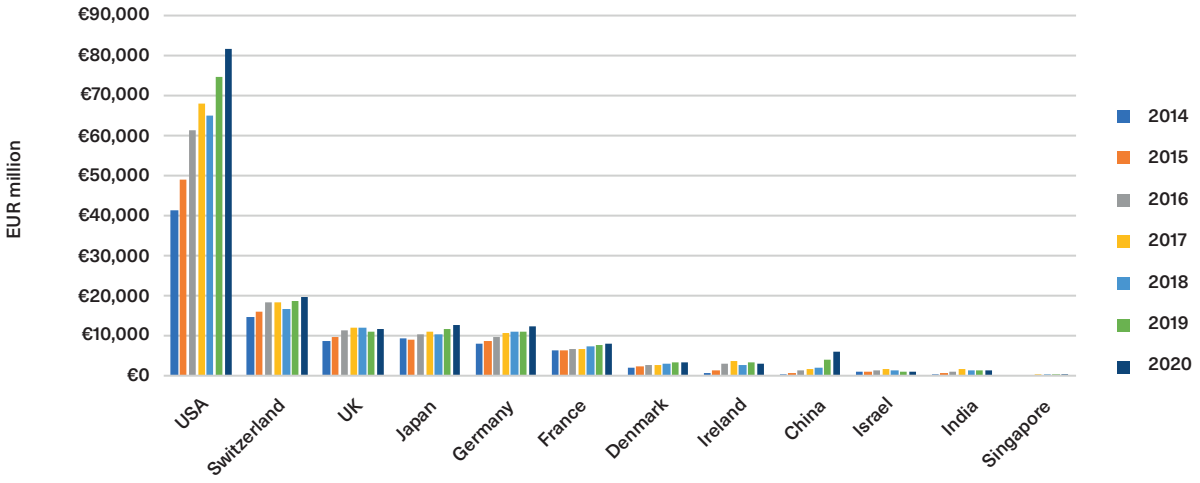

Figure 8: Total R&D expenditure by company HQ between 2014 and 2020. Source: Calculation by study authors by data from EU industrial R&D investment scoreboard 2014-2020

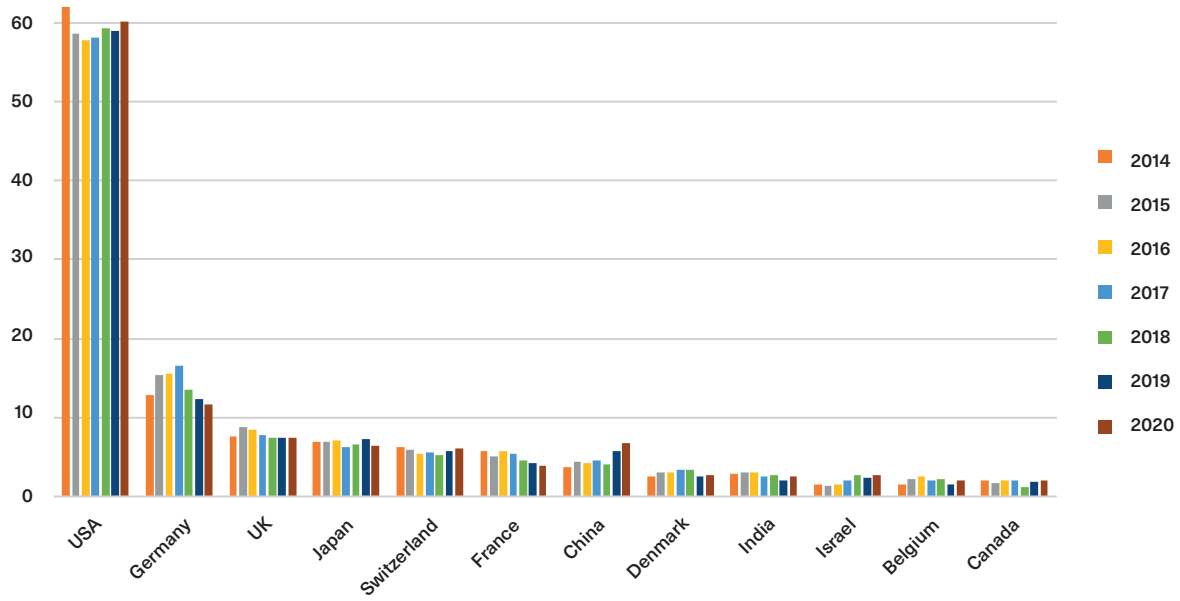

Figure 9: R&D location/ Patent inventor location for BioPharma firms with highest R&D investments worldwide. Source: Calculation by study authors by data from EU industrial R&D investment scoreboard 2014-2020 and patent data from ORBIS Intellectual Property (Bureau van Dijk)

Private capital market financing

We used Pitchbook for national benchmarking of the pharmaceutical and biotechnology sectors, with data spanning the period 2000-2021. For these analyses, the proprietary Pitchbook industry categorisations were used to define sectors to ensure comparability over time. It is important to note that the biotech category includes both medical and non-medical biotech companies. Up to 44% of the medical biotech companies are listed as performing 'drug discovery', i.e. researching and developing of new drug products, including identification, screening, and efficacy testing of drug candidates. Other companies are involved in health-related activities such as genetic engineering and artificial tissue growth, or the development of platform technologies (see methodology for Pitchbook definitions).

Measured by deal count and investment size, both sectors have shown steady growth, with steeper growth associated with the biotech sector (Figure 10). The growth in venture capital (VC) and initital public offering (IPO) investments since 2000 is similar between biotech and

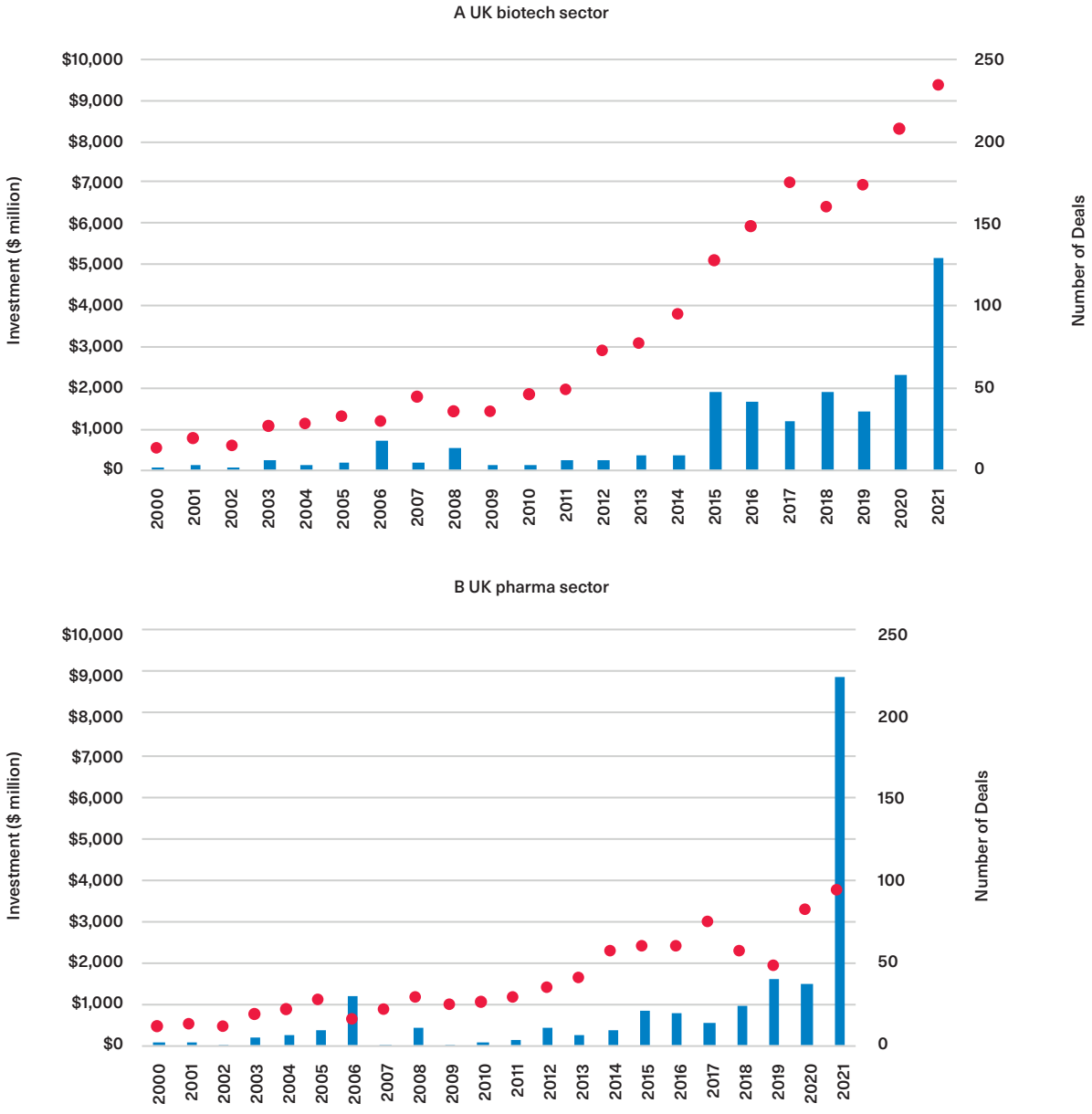

Figure 10: Number of companies (bar chart) and median private capital market investment size (line chart, $ million) between 2000 and 2021. Source: Calculation by study authors by data from Pitchbook

pharma (data not shown). Growth in VC investments have been driven by early and late-stage investments (Figure 11). Most company exits involve merger and acquisition, followed by IPO. There are low levels of bankruptcy and buyout (Figure 12).

When looking at Pitchbook pharmaceutical and biotechmnology industry data across 20 countries (2000-2021), the UK pharmaceutical sector ranks seventh in total capital invested through private equity, VC, public offering, and Mergers & Acquisitions (M&A), behind the USA, China, Switzerland, Germany and France (Figure 13). The UK biotechnology sector ranks fifth, with an upward trend in 2021. The UK pharmaceutical industry ranks eight in IPO funding (data not shown). The USA and China dominate the ranking for VC funding, with consistent increases over recent years. The UK biotechnology and pharmaceutical sectors rank third, with a recent upward trend (Figure 14 and 15).

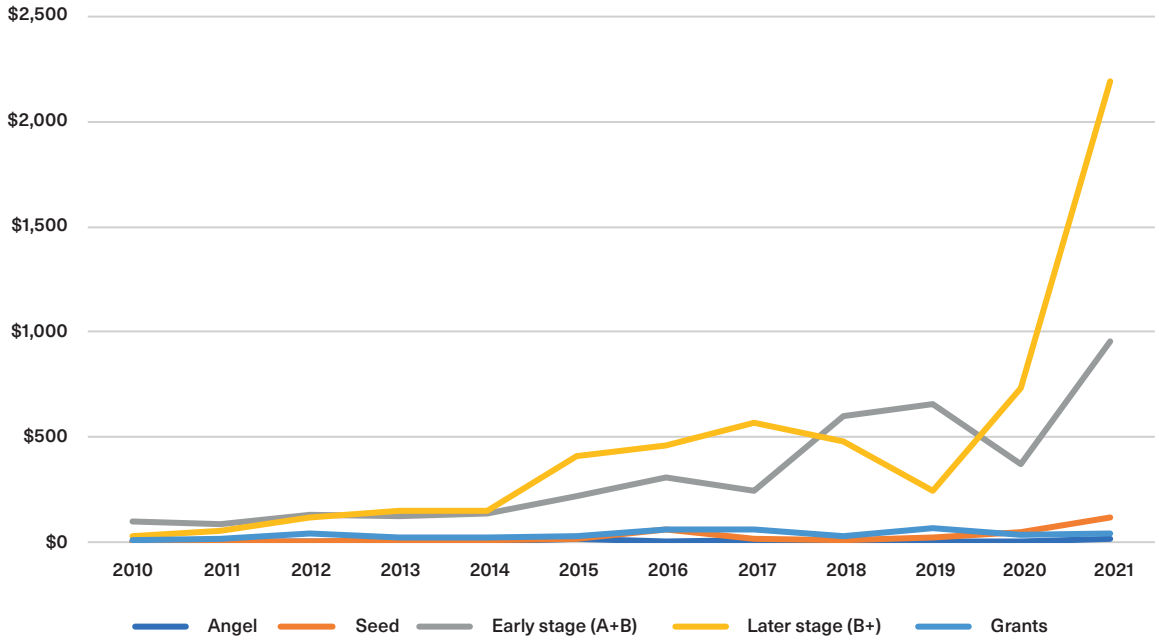

Figure 11: Sum of VC funding between 2000 and 2021 according to VC capital round/stage: comparison between UK biotech and UK pharma sectors ($ million). Source: Calculation by study authors by data from Pitchbook

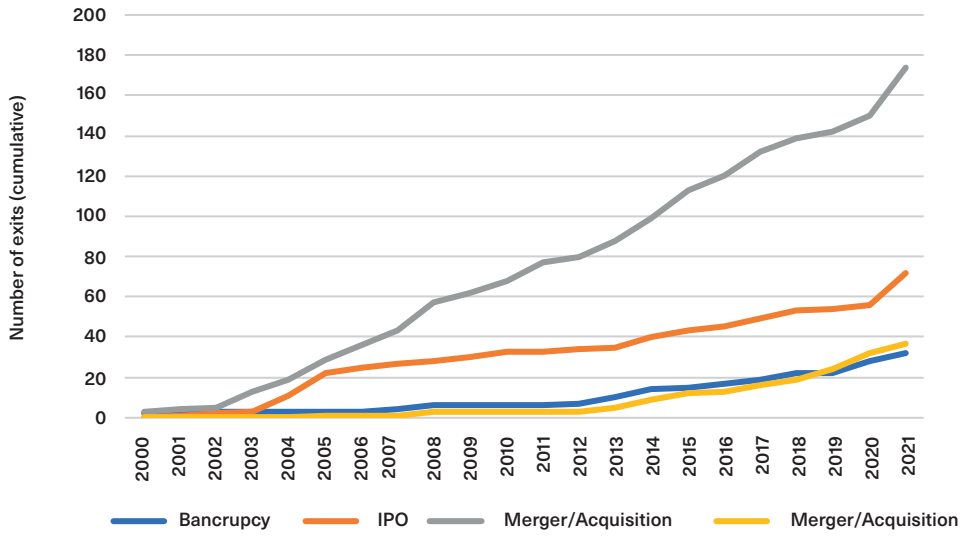

Figure 12: Cumulative number of company exit types between 2000 and 2021. Source: Calculation by study authors by data from Pitchbook

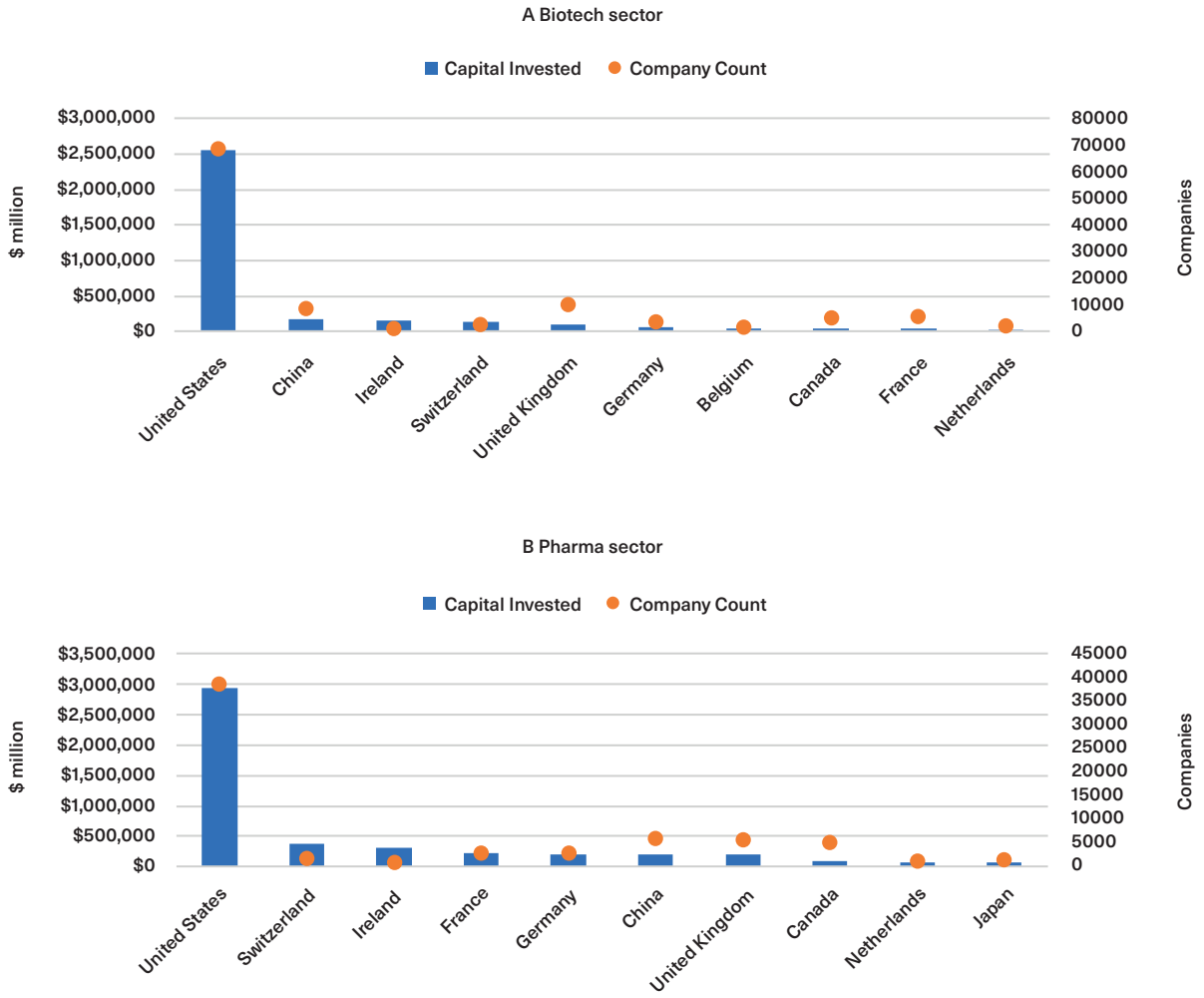

Figure 13: Total private capital market investment (bar chart, $ million) and number of companies (line chart).
Source: Calculation by study authors by data from Pitchbook

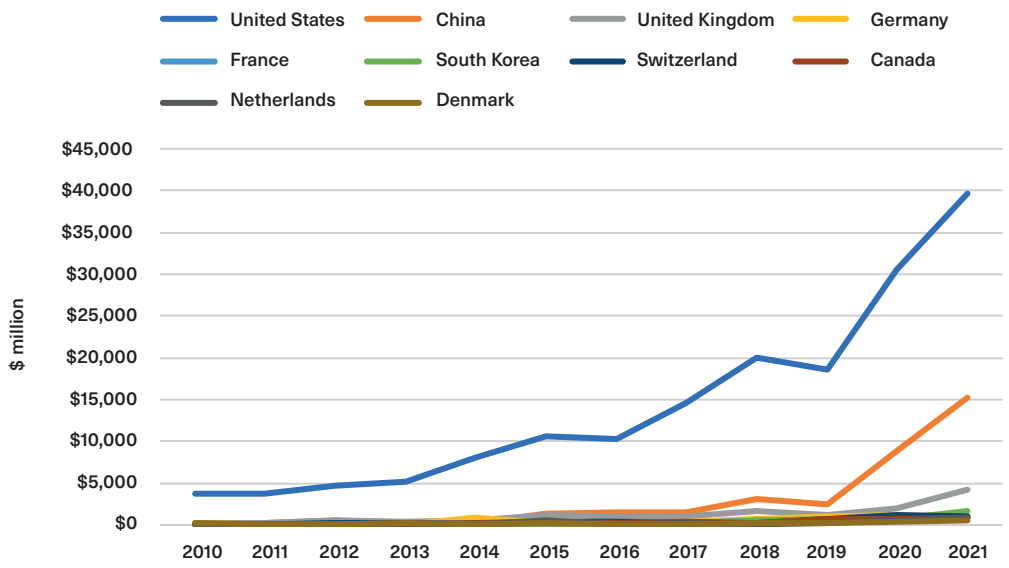

Figure 14: VC funding for biotech sector by country between 2010 and 2021 ($ million). Source: Calculation by study authors by data from Pitchbook

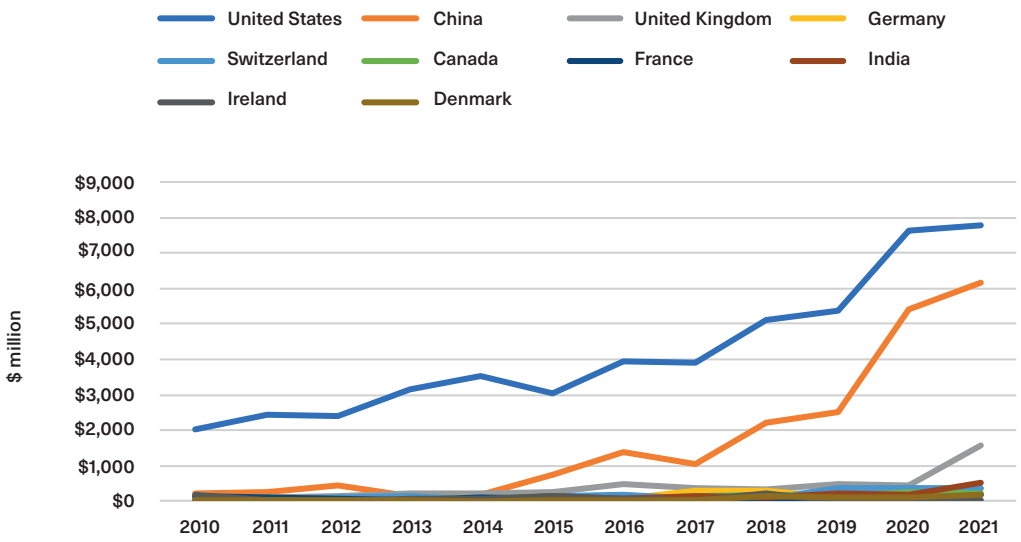

Figure 15: VC funding for pharma sector by country between 2010 and 2021 ($ million). Source: Calculation by study authors by data from Pitchbook

Section 3: Opportunities and capabilities

In part 3 we take a deeper look at the current structure of the UK biopharma industry and its R&D activities and capabilities. We then discuss its opportunities and threats.

Industry structure

The UK's biopharma sector consists of around 977 firms, of which around 80% are small to medium sized companies (SMEs) and 60% are headquartered in the UK. The sector has many international ties, with headquarters in countries including USA (140 companies), India (34), Germany (34), Japan (30), Switzerland (25), France (22) and Ireland (21).

In 2021, the sector employed 393,627 people and had a turnover of £149.8 billion. There has been steady growth across all indicators, including employment, turnover, and R&D investment, with positive five-year compound annual growth rates between 2016 and 2021. However, GVA for the whole sector peaked in 2020 at £62.6 billion, then decreased to £50 billion in 2021. Similarly, GVA per employee peaked in 2020 at £157,000 and subsequently declined in 2021 (see Table 2). GSK and AstraZeneca, the two leading pharmaceutical companies headquartered in the UK, contribute over 40% to all sector economic and performance indicators (Figure 16). This report compiled economic information on GlaxoSmithKline plc before the demerger and split into GSK plc (pharmaceutical business) and Haleon plc (consumer health business) announced at the beginning of 2022.

Although biopharma companies are located across all UK regions, clusters stand out in north-west and south-east England. There is a clustering of company and manufacturing locations around financial and scientific centres: (1) the London, Cambridge, Oxford and south-east England more widely, and (2) Liverpool and Manchester. Other clusters include Newcastle and north-east England, and the Edinburgh – Glasgow belt (Figure 17). The highest GVA contribution of pharmaceutical industry can be found in clusters around London (11.9%), East of England (12.3%), south-west England (9.6%), and north-west England (38%). [53]

The Oxford, Cambridge and London 'golden triangle' includes globally leading R&D clusters such as the Oxford Biotech Network, with over 250 businesses, and the area around Cambridge, where both AstraZeneca and GSK have significant R&D facilities. Located between these two clusters are the UK's first open innovation biopharma campus, Stevenage Bioscience Catalyst, and a major Roche R&D hub in Welwyn Garden City. A 2020 report for Enterprise Ireland estimated that 38% of the output and 43% of the UK pharmaceutical turnover is generated here. The north-west England region contains biopharma R&D facilities such as Alderley Park, near Macclesfield, the UK's largest single site life science campus. [53]

	Employment	Turnover (£m)	GVA (£m)	GVA/employee (£m)	R&D investment (£m)
2016	359,317	£109,586	£41,159	£0.115	£11,201
2017	370,946	£117,470	£42,821	£0.115	£11,099
2018	379,633	£124,789	£47,906	£0.126	£11,444
2019	390,191	£127,574	£50,923	£0.131	£12,223
2020	399,896	£136,316	£62,596	£0.157	£12,168
2021	393,627	£149,808	£49,979	£0.127	£14,833
CAGR rate	**+ 1.84%**	**+ 6.45%**	**+ 3.96%**	**+ 2.08%**	**+ 5.78%**

Table 2: BioPharma ecosystem and economic indicators from 2016 to 2021.

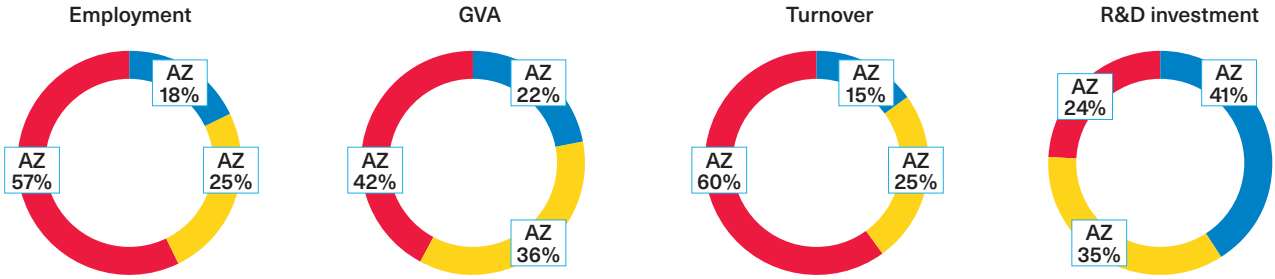

Figure 16: Contribution of GlaxoSmithKline (GSK) and AstraZeneca (AZ) to 5-year employment, GVA, turnover, and R&D investment (2016-2021)

Figure 17: Heat maps of the geographical distribution of UK biopharma sector companies. Panel A: locations of company headquarters. Panel B: locations of manufacturing sites. Panel C: locations of supply sites. Source: Project database with data from MHRA and Bureau van Dijk

The biopharma industry can be divided into five subsectors according to whether they are involved in researching and developing pharmaceutical products, manufacturing them, importing and supplying them, or any combination of these (see box 8). Its key features are:

- The largest sector by number of companies is the biopharma sector, i.e. businesses involved in developing and/or producing pharmaceutical products. This predominantly comprises micro- (337, 57%) and small-sized companies (122, 21%). In contrast, the biopharma and manufacturing sector, and biopharma and supply sector, comprise a relatively small number of companies, of which approximately half are large companies (Table 3).
- Overall, companies in the biopharma sector are relatively young, with approximately 70% incorporated in the last 20 years (data not shown). This might explain why it is comprised largely of micro- and small-sized companies. Understanding the factors that may lead to at least some of these companies growing to become significant global players is therefore important.
- The biopharma and manufacturing sector is responsible for the highest level of employment (approximately 60%).
- The two subsectors that concern drug manufacturing are responsible for the highest economic contribution in terms of GVA (Figure 18). The biopharma and manufacturing sector has the highest GVA, with £37.4 billion and a 3.36% compound annual growth rate (CAGR) since 2016. This is followed by the manufacturing and biopharma sectors with GVAs of £6.7 billion and £3 billion respectively. The supply sector shows the highest growth since 2016 with a CAGR of approximately 15%.
- The biopharma and supply sector has the highest GVA/employee, closely followed by the biopharma and manufacturing sector. Both sectors have seen growth since 2016 of approximately 8% and 1.3% CAGR since 2016. The other sectors are characterised with relatively low productivity.

BOX 8. CATEGORISING THE UK BIOPHARMA INDUSTRY

1. Biopharma: 591 businesses involved in developing and/or producing pharmaceutical products. Prominent examples include drug developers Hikma (UK), Galen (UK), Amryt (UK), Vertex (USA), Astellas (Japan), Eli Lilly (USA), and drug development service firm Abcam (UK).
2. Manufacturing: 141 businesses with import and manufacturing license for medicines in the UK with registered activity of medicines manufacturing. Prominent examples include Intertek (contract manufacturer, UK), Croda (contract manufacturer, UK), Almac (contract manufacturing, UK), Bio Products Laboratory (blood product manufacturer, UK), Owen Mumford Holdings (contract manufacturing, UK), BOC (gas producer, Linde Ireland), Siemens Healthcare (drug development support, Siemens Germany), Patheon UK (contract manufacturer, Thermo Fisher USA), Sigma Aldrich (contract manufacturer, Merck KG Germany), Parexel (drug development support, USA).
3. Supply: 105 businesses with import and manufacturing license for medicines in the UK with registered activity of import, quality control and packaging. Prominent examples include Lexon (wholesaler, UK), Bap Pharma (wholesaler, UK), Ivor Shaw (wholesaler, UK), Beachcourse Limited (wholesaler, AmerisourceBergen USA), Alcura UK (wholesaler, AmerisourceBergen USA), Ecolab (contract manufacturer, Ecolab USA)
4. Biopharma and manufacturing: 82 businesses involved in developing and/or producing their own pharmaceutical products and with registered activity of medicines manufacturing. Prominent examples include GlaxoSmithKline (drug developer, UK), AstraZeneca (drug developer, UK), Reckitt Benckiser (frug developer, UK), Napp Pharmaceuticals (drug developer, UK), Oxford Biomedica (drug developer, UK), Pfizer (drug developer, USA), Seqirus (drug developer, CSL Australia), Novartis (drug developer, Switzerland), Baxter, (drug developer, USA), Eisai (drug developer, Japan), Teva (drug developer, Israel), Accord (drug developer, India).
5. Biopharma and supply: 58 businesses involved in developing and/or producing their own pharmaceutical products and with registered activity of import, quality control and packaging. Prominent examples include Clinigen (drug development support, UK), Mawdsley-Brooks (wholesaler, UK), Atnahs Pharma/ Pharmanovia (drug developer, UK), Mundipharma (drug developer, UK), Roche (drug developer, Switzerland), 3M (drug development support, USA), Janssen-Cilag (drug developer, Johnson & Johnson USA), Bristol-Myers Sqibb (drug developer, USA), Chiesi (drug developer, Italy), Gilead (drug developer, USA), Abbvie (drug development, USA), Sandoz (drug development, Novartis Switzerland).

Characteristics	Total	Biopharma	Manufacturing	Supply	Biopharma & Manufacturing	Biopharma & Supply
Company number	977	591	141	105	82	58
Number of SMEs (%)	800 (82%)	540 (91%)	105 (75%)	89 (85%)	36 (44%)	30 (52%)
UK HQ (%)	562 (58%)	376 (64%)	72 (51%)	65 (62%)	30 (37%)	19 (33%)
Employment 2021 (5-year CAGR rate)	393,627 (1.84%)	34,808 (3.04%)	90,201 (1.83%)	11,486 (7.74%)	247,091 (1.59%)	10,041 (-1.29%)
Turnover 2021 (£m) (5-year CAGR rate)	£149,808 (6.45%)	£23,574 (7.57%)	£13,724 (5.19%)	£4,245 (13.92%)	£101,025 (6.38%)	£7,239 (3.17%)
GVA 2021 (£m) (5-year CAGR rate)	£49,979 (3.96%)	£2,973 (4.79%)	£6,722 (5.08%)	£1,020 (14.96%)	£37,430 (3.36%)	£1,833 (6.68%)
GVA/employee 2021 (£m) (5-year CAGR rate)	£0.127 (2.08%)	£0.085 (1.7%)	£0.075 (3.19%)	£0.089 (6.7%)	£0.151 (1.74%)	£0.183 (8.08%)
R&D investment 2021 (£m) (5-year CAGR rate)	£14,833 (5.78%)	£1,169 (0.31%)	£288 (2.18%)	£10 (13.5%)	£12,855 (6.57%)	£511 (6.57%)

Table 3: Overview of characteristics of five biopharma sectors. Source: Project database with data from Bureau van Dijk

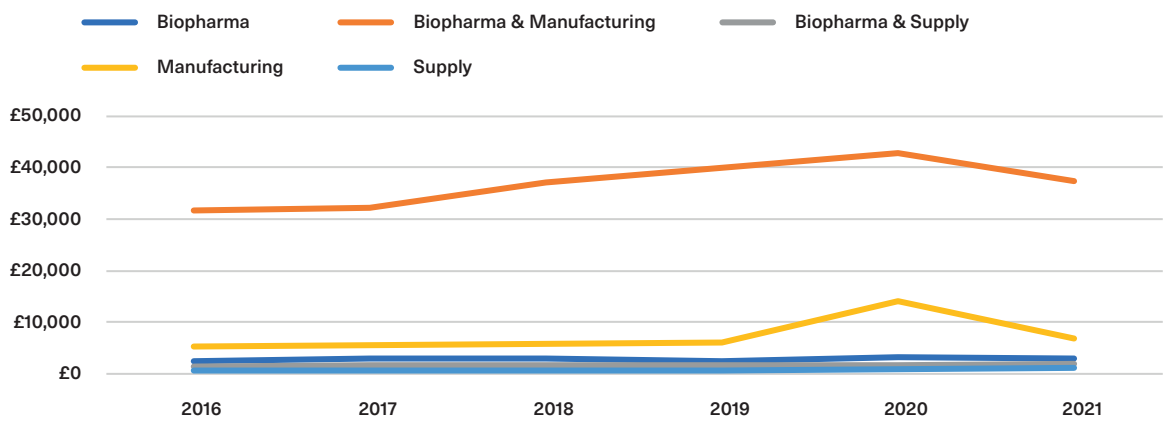

Figure 18: Time series of the estimated GVA for the different sub-sectors Source: Project database with data from Bureau van Dijk

Research and development

R&D activity

Most companies are research active and only 23% have no published measurable R&D output yet. However, only a relatively small proportion of UK biopharma sector companies have managed to go through the full development cycle leading to medicinal product approval (12%). The largest proportion of all companies was found to be patenting stage (34%), while 25% of all companies entered clinical trials (Figure 19).

Unsurprisingly, there seems to an association between company size and stage of R&D output on the development pathway. While micro-sized companies are lagging and mainly operate at early R&D stage, e.g. patent stage, large-sized companies are associated with late-stage clinical activity and drug approval to a higher degree (Figure 20).

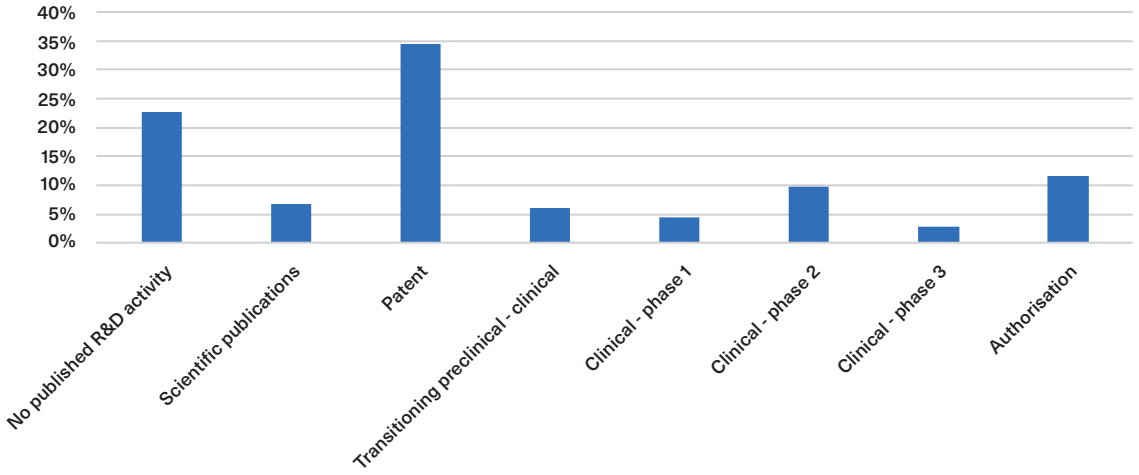

Figure 19: Percentage of all companies in different phases of R&D pipeline. Data sources: Project database with data from Clarivate Web of Science, Elsevier Scopus, Clinicaltrials.gov, EudraCT, ISRCTN registry.

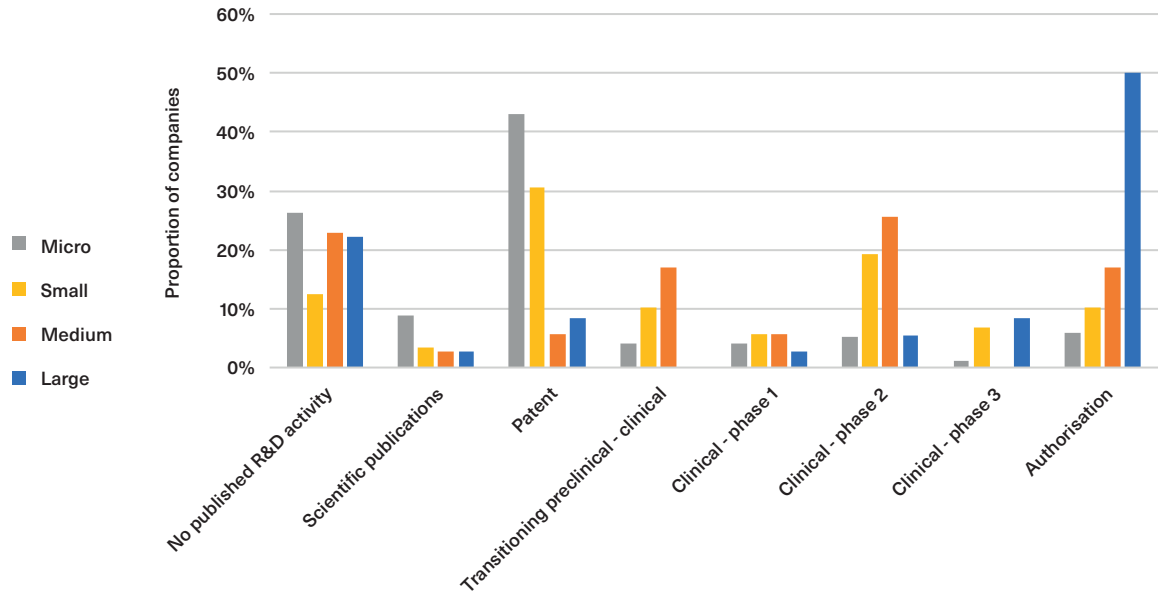

Figure 20: Percentage of companies in different phases of R&D pipeline - comparing company subsets based on company size. Data sources: Project database with data from Clarivate Web of Science, Elsevier Scopus, Clinicaltrials.gov, EudraCT, ISRCTN registry.

R&D location

In line with previous studies and the methodology in the EU Industrial R&D Investment Scoreboard, we used patenting data to understand the location of biopharma R&D activity. [60] In other economic sectors, the use of patent data to measure innovation is debated [61] but the patenting system in the pharmaceutical sector plays a vital role in protecting intellectual property to recoup R&D investment costs [62] and the location of patent filing provides at least a proxy for R&D activity.

Patenting activity was analysed for the following categories (Figure 21):

- Home activity: UK headquartered companies filed 9,425 patents with patent inventors in the UK. This is estimated to equate to an R&D expenditure of $26.4 billion. Around $20 billion of this expenditure can be attributed to AstraZeneca and GSK (data not shown).
- Outward activity: UK headquartered companies filed 5,700 patents with patent inventors outside the UK. This is estimated to equate to an R&D expenditure of $57.9 billion. Most of this activity and expenditure is directed to the USA, followed by the EU, notably Sweden, Belgium, and Italy (Figure 22). AstraZeneca and GSK perform more than half their R&D activity in the USA measured this way, equivalent to approximately $30 billion (data not shown).
- Inward activity: Biopharma companies with headquarters overseas filed 8,112 patents with patent inventors in the UK. This equates to an R&D expenditure of $42.6 billion. Large global pharma companies are amongst the companies with the highest R&D activity in the UK. These include 3M, Roche, Bayer, Johnson & Johnson, Sanofi, Merck, Pfizer, and Novartis. While in absolute terms these companies contribute high levels of R&D in the UK, relative to their total R&D activity, they only spend a small proportion of their total R&D activity in the UK (approximately 10%).

A previous study that found that between 2001 and 2005 46.8% of pharmaceuticals patenting activity by UK firms was associated with inventors in the UK [63], lower than other European nations, including France (64.2%) and Germany (65.5%). According to the above outlined findings UK headquartered firms conduct 62% of their patentable R&D activity in the UK.

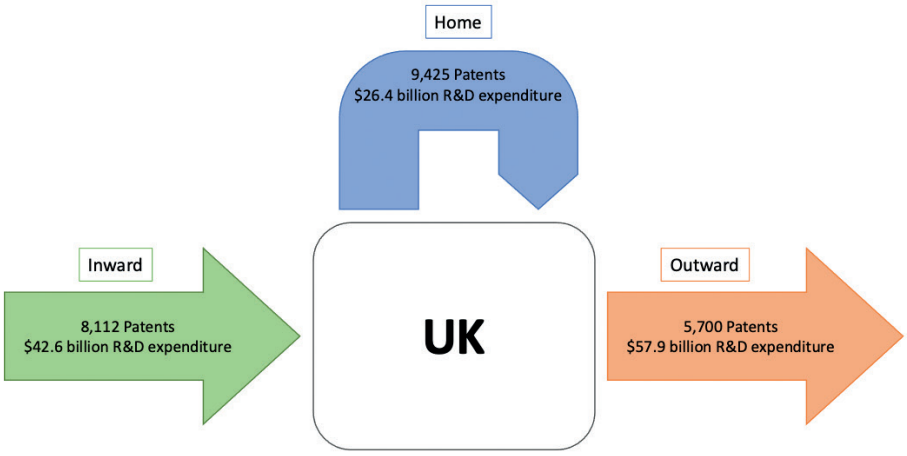

Figure 21: Patenting activity of UK biopharma companies between 2016 and 2021 according to R&D location, i.e. the location of the patent inventor. The patenting activity of UK BioPharma project database was analysed on headquarter level, which included companies with UK and overseas headquarters. Patents (live, priority date 2016-2021, family size ≥2) associated with the companies were pooled and analysed for patent inventor location. R&D expenditure for the estimation of R&D investment flow was available for 227 of 652 companies in the database (35%). Source: Project database with data from Bureau van Dijk

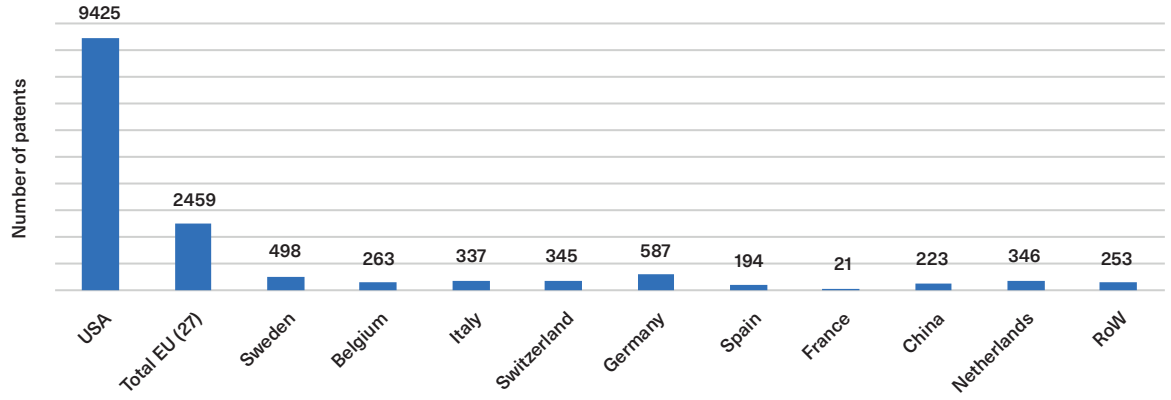

Figure 22: Outward activity in number of patents. Source: Project database with data from Bureau van Dijk

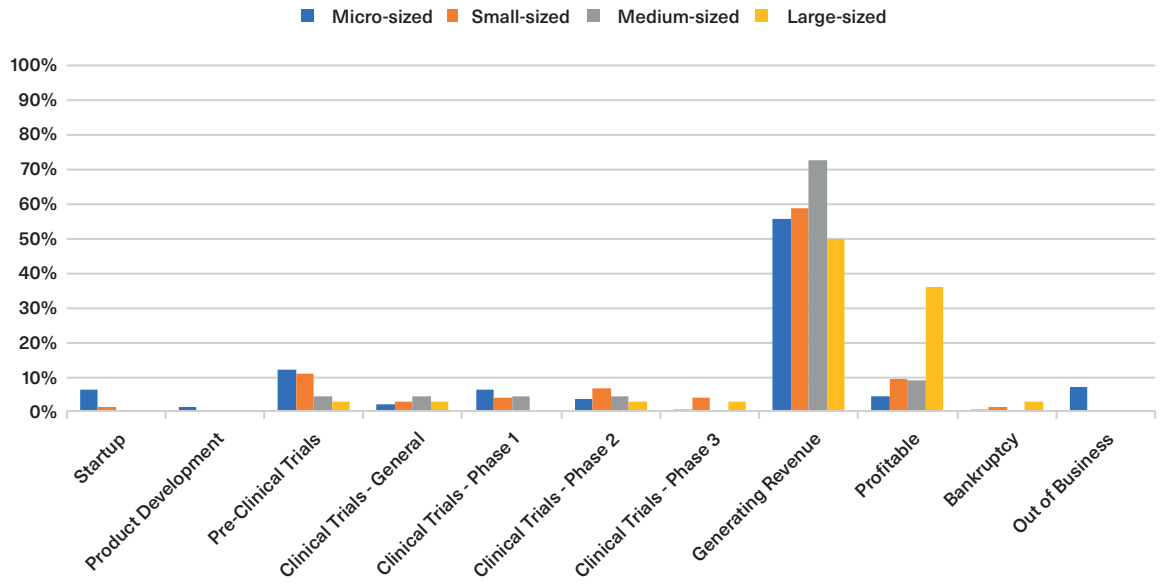

Figure 23: Proportion of private capital market funding deals according to company size and business stage/ product development stage. Source: Project database with data from Pitchbook

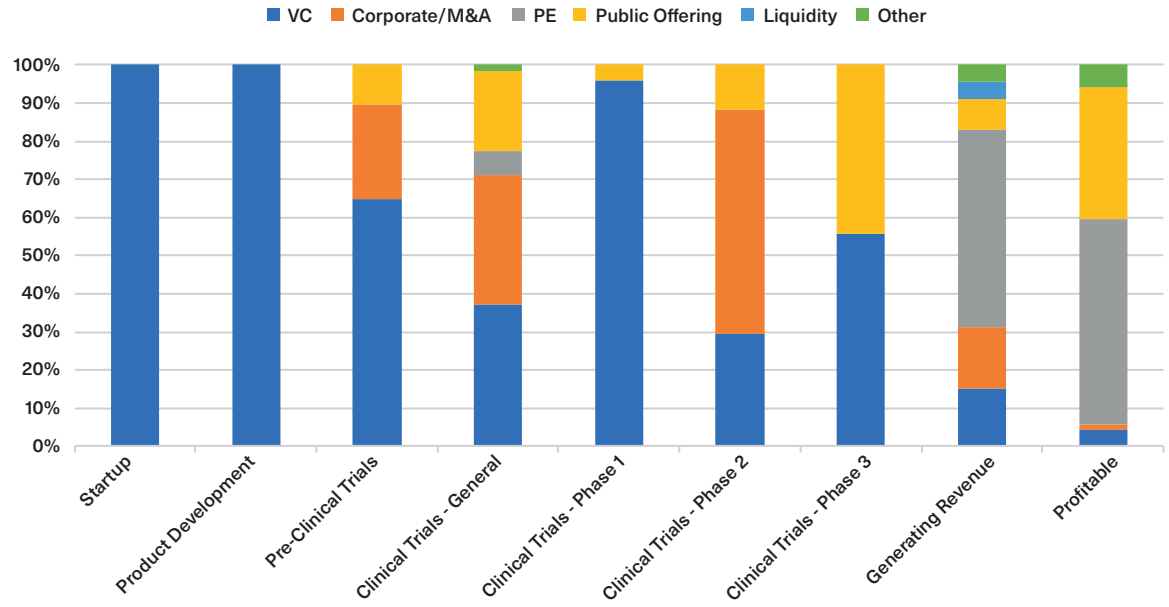

Figure 24: Proportion of private capital market funding according to type of funding and business stage/ product development stage. Source: Project database with data from Pitchbook

Investment

We used Pitchbook as a data source for private capital market investments and funding sources for biopharma (including manufacturing and supply) companies in our project database (Pitchbook coverage was 63%). We did not investigate public funding for biopharma R&D projects in this study.

A total of 1498 investment deals of any kind were identified, amounting to $47.6 billion investment and a median deal size of $3.56 billion. Companies raised the highest investment through private equity (PE) deals ($27.9 billion), public offerings ($10.9 billion), venture capital (VC $9.9 billion), and corporate investment ($8.5 billion).

The highest proportion of deals was secured when companies start generating revenue, but there were fewer investment deals at the start-up, product development, pre-clinical testing, and early clinical testing phases (Figure 23). For small- and micro-sized companies, funding of early preclinical and clinical testing is more important, shown by slightly higher funding in early phases (data not shown). Proportionally, early preclinical, and clinical testing is mainly reliant on VC funding.

Later phases of clinical development see funding via corporate investments (e.g. mergers and acquisitions) and public offerings like IPO. Private equity deals mainly occur during late-stage clinical development and when revenue is generated (Figure 24).

Manufacturing

The location and structure of the manufacturing sector was mapped using manufacturing approval data from the MHRA, which is the regulator responsible for authorising drug manufacturing sites in the UK.

The analysis identified 563 licensed manufacturing sites. Private pharmaceutical companies have a total of 509 unique manufacturing sites across the UK. Other licensed manufacturers include 40 NHS hospital and government organisations and 14 university facilities or charity organisations. These are largely in manufacturing using biological ingredients and advanced therapies including gene and cell therapies (Figure 25).

Commercial medicines manufacturing by pharmaceutical sector is spread across 509 sites, both manufacturing sites (298) and supply-only sites engaged in import and distribution, packaging, and quality testing (211). These are mainly located in Northwest England, London, Northeast, England, Midland and Scotland. These manufacturing sites mainly produce medicines with chemical ingredients (147) and active ingredients (63). Less than 10% of sites produce biological products and more advanced therapies (Figure 26). The majority of supply-only sites are concerned with import and distribution (161) and packaging (67) (Figure 27).

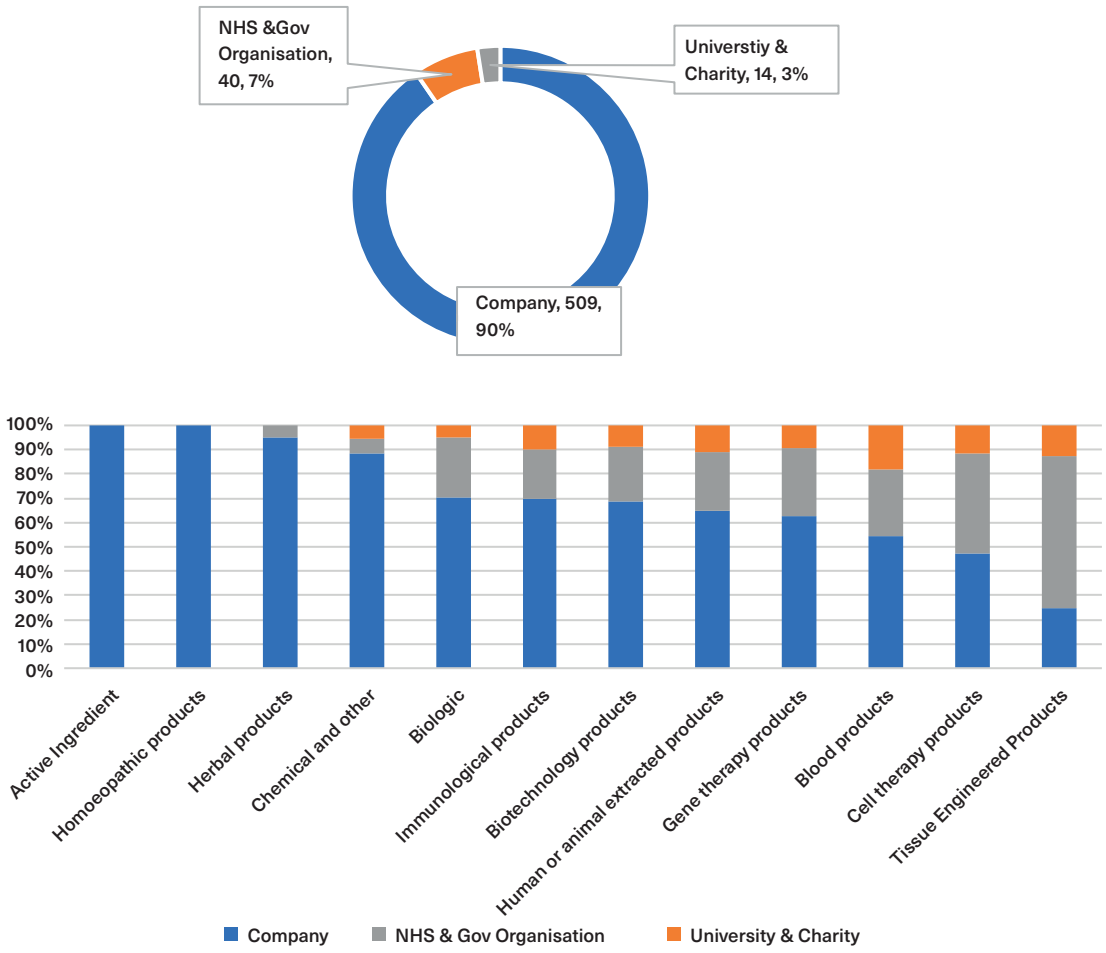

Figure 25: Number of manufacturing sites according to ownership (top panel), and the manufacturing capability per product group and ownership (bottom panel). Source: Project database with data from MHRA database

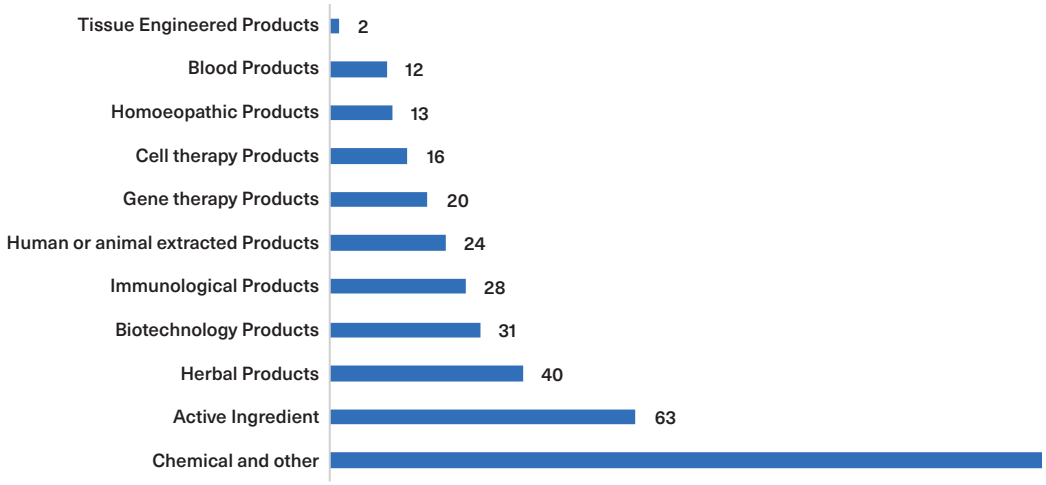

Figure 26: Manufacturing capabilities of pharmaceutical industry in UK. Total number of manufacturing sites = 298. Individual sites can have two or more capabilities. Source: Project database with data from MHRA database

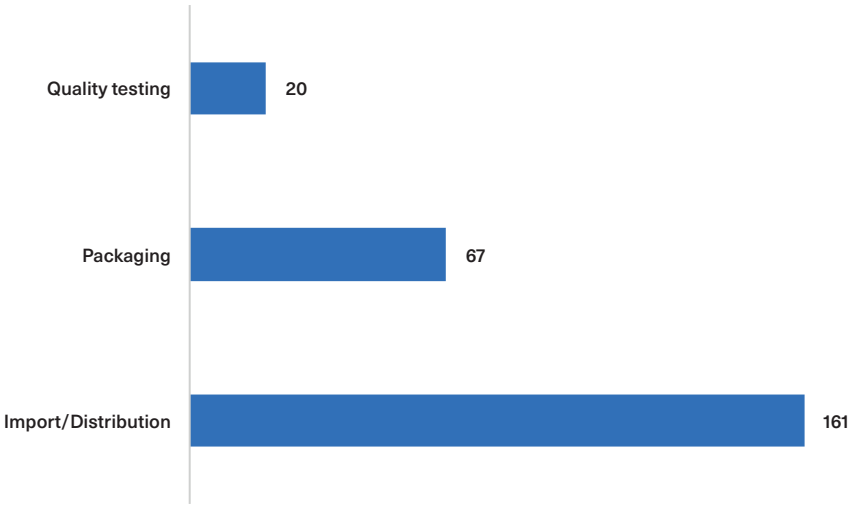

Figure 27: Supply capabilities of pharmaceutical industry in UK. Total number of supply sites = 211. Individual sites can have two or more capabilities. Source: Project database with data from MHRA database

Opportunities and threats

The science and R&D environment for the UK's biopharma sector has a number of strengths and opportunities to sustain and improve on its performance in the future. The university sector is highly ranked globally, most UK biopharma companies are R&D active, and there is still relatively high inward investment to conduct R&D in the UK. There are important opportunities to foster the newer companies providing data science, artificial intelligence, diagnostics, digital health, and other innovative technologies supporting drug development.

There are also weaknesses and threats. The R&D output of companies tends to be at early stage and companies face problems securing investment to move it forwards through the development pipeline. There are also several other countries with stronger growth in R&D investment and better translation into commercialised products. The decline in the clinical trial infrastructure since 2017 has also inhibited companies from conducting drug development activity in the UK.

The business environment for biopharma also presents strengths and opportunities – the presence of two global pharmaceutical companies, funding for translational research, the potential for economic impact by small and young companies with high R&D activity. But there are also risks associated with dominance of micro- and small-sized companies in the biopharma sector, where there is a tendency to sell to non-UK companies as soon as revenue generation begins.

For biopharma manufacturing and trade, the weaknesses and threats arguably outweigh the strengths. The shift in certain areas of manufacturing away from the UK is clear and is unlikely to be reversed for low value products. To counter this decline, the UK needs to gain and maintain competitive advantage in manufacturing high value products, such as advanced therapeutics. **Opportunities exist here, as well as in developing the future technologies for advanced manufacturing processes.**

There are concerns about the UK's regulatory and policy environment. While there is a strong desire to grow the UK's biopharma and life sciences capabilities, and in recent months certain policy initiatives have been put in place to help support this, there remain concerns over divergence from European regulatory frameworks, leading to potentially increased costs for biopharma companies and potentially slowing access to new medicines for the UK's population.

	Business Environment	Science and R&D	Manufacturing and Trade	Regulatory and Policy
Strengths	• Two global top biopharma companies AstraZeneca and GSK are headquartered in the UK • Sector's total employment and turnover remain relatively stable over the last 10 years • Clusters of scientific and economic excellence allow for networking • VC funding is available to fund translational research, especially for biotech companies	• Highly ranked university sector • Most UK biopharma companies are R&D active • High inward investment to conduct R&D in the UK	• Historically strong sector in medicines manufacturing • Manufacturing capabilities are situated around the same geographic clusters	• UK government has set out a policy agenda for life sciences and biopharma manufacturing • Strong industry bodies • High reputation for regulatory bodies MHRA and NICE • National health system for single procurement (with local fragmentation)
Weaknesses	• Biopharma sector is characterised by micro-sized and small-sized companies • Without AZ and GSK, the economic value added is relatively low	• R&D output by UK biopharma companies is at early stage and it is unclear if the current R&D investment will ever create new therapies or economic benefit • Clinical trial infrastructure has declined since 2017 • High demand for appropriate life-sciences real estate	• Big shift from UK manufacturing industry to Far East, USA, Japan, Singapore, Switzerland, and Ireland. • Reported and perceived skill shortage in some fields, e.g. data science.	• Regulatory uncertainty after Brexit • No participation in European unitary patent system • Potential changes to data protection framework that protects authorised medicines beyond patent expiry
Opportunities	• Potential for high economic impact by small and young companies with high R&D activity in the future.	• Fostering active R&D and supporting the growth of companies involved in new drug development technologies, e.g. data science, artificial intelligence, diagnostics, digital health	• Gain and maintain competitive advantage in manufacturing of high value products, e.g. advanced therapeutics • Championing innovation in manufacturing process, e.g. Continuous Manufacturing	• Foster new international cooperation after Brexit • Create a fully integrated approach for developing, regulating, and fostering pharmaceutical innovation (NIHR, NHS, MHRA, NICE, DHSC) • Champion innovative regulation and integration of new technical advances regarding data science, AI, diagnostics, digital health, real world evidence
Threats	• High economic risk associated with micro- and small sized companies in the biopharma sector	• Competitor countries with stronger growth in R&D investment and better translation	• Highly competitive countries on lower value medicine manufacturing, e.g. China, India	• Without a formal reliance to other regulatory systems, UK might fall behind in terms of authorisation, which could affect patient access • UK IP system might lose international relevance

Table 4: Strengths, weaknesses, opportunities and threats for UK biopharma

Section 4: Conclusions and recommendations

Overall, the goal for government must be an integrated national life sciences R&D ecosystem which supports drug discovery, early clinical development, and uptake into healthcare, reduces transaction times and costs, and ultimately produces more attractive investment opportunities.

Investing in and adopting innovative drugs and other healthcare technologies creates a virtuous circle, as pointed out by ABPI in its 2022 review of the state of the UK life sciences sector. [8] Such a virtuous cycle should also consider a return on investment for public investment not only in terms of economic benefits and job opportunities, but also in terms of sustainability of the national healthcare system and improvement of population health.

The UK offers many advantages for life science businesses: opportunities for collaboration with the NHS in R&D, globally leading science from academic institutions, access to talent in science and technology, well-developed sources of early-stage research support, a growing investor base, a respected regulator in the MHRA, and a number of geographical biopharma clusters attracting international talent and innovation. [64]

But to enhance this ecosystem, it needs to be as efficient and effective as possible, integrating both the public – NHS and academia – and private sectors, and able to coordinate its activities from early-stage science to adoption into healthcare practice. Not only does this require the right policy environment to be created, there also needs to be continuity in policy making and in public funding and support to instil greater confidence in research organisations, companies and private investors. [2]

BOX 9. CREATING A VIRTUOUS CIRCLE.

A thriving commercial environment that values technological innovation in the life sciences reinforce a country's position as a priority market for global pharmaceutical companies. This in turn attracts investment from venture capital, private equity, government funding, philanthropy, and other sources. Increased funding sustains research to support the next wave of innovation. Clinical trials to evaluate the impact of life science innovation contribute to the economy and raise the likelihood that patients will receive early access to beneficial new treatments. Progression from clinical trials to approval and launch stimulates manufacturing, generating economic benefits and job opportunities.

Source: PWC and ABPI (2022) Life Sciences Superpower.

Several reviews over the last few years have highlighted that support should also be targeted on high value products and services in areas where the UK has particular strengths. [2,25] These include:

- The discovery of novel chemical compounds through biological screening and structural biology.
- Enabling technologies for drug discovery, such as large-scale human omics, cellular assay methods and precise genome editing.
- Data-driven life sciences, with a thriving ecosystem of start-ups and small companies. However, there is some concern that the ecosystem could be better integrated, with government agencies and NHS bodies presenting a more unified approach to access projects, contracts and data. [64]
- The UK has a rich data legacy of disease cohorts, which are valuable sources of well-validated drug targets that can be further profiled using advanced biomarker technologies.
- Some experts see potential in commercial repurposing, where existing compounds are developed for new therapeutic purposes. [65]

The opportunities vary across different stages of the biopharma development process. [8] In the early research phase, the UK has emerging companies but the need help to grow into medium-sized companies before they become foreign acquisitions. During the preclinical and clinical development phase, the UK has the potential to excel in clinical trials by reducing setup times, leveraging existing data capabilities, and integrating clinical research into routine care. The drug manufacturing sector needs to be revitalized, focusing on higher value products and advanced therapy medicinal products (ATMPs), where there are UK strengths. While the UK faces challenges in access to and adoption of new drugs and biopharma products, various levers are available to increase access, while the scale of the NHS as a customer should be leveraged as an attractive market.

In the previous section we concluded that while the UK performs well on basic science, attention is needed to grasp the opportunities and translate potential innovations into commercialised products and services. Section 4 sets out our recommendations, drawing on our own empirical research on the biopharma sector, stakeholder interviews, and our assessment of previous policy and other recommendations for the sector. The latter is based on a review of 208 policy recommendations found in 33 reports and submissions on the state of the UK's life sciences, published between 2015 and 2023. Figure 28 provides an overview of the main areas where stakeholders suggested policy intervention is needed to support the sector. [1] Our recommendations are summarised in table 5.

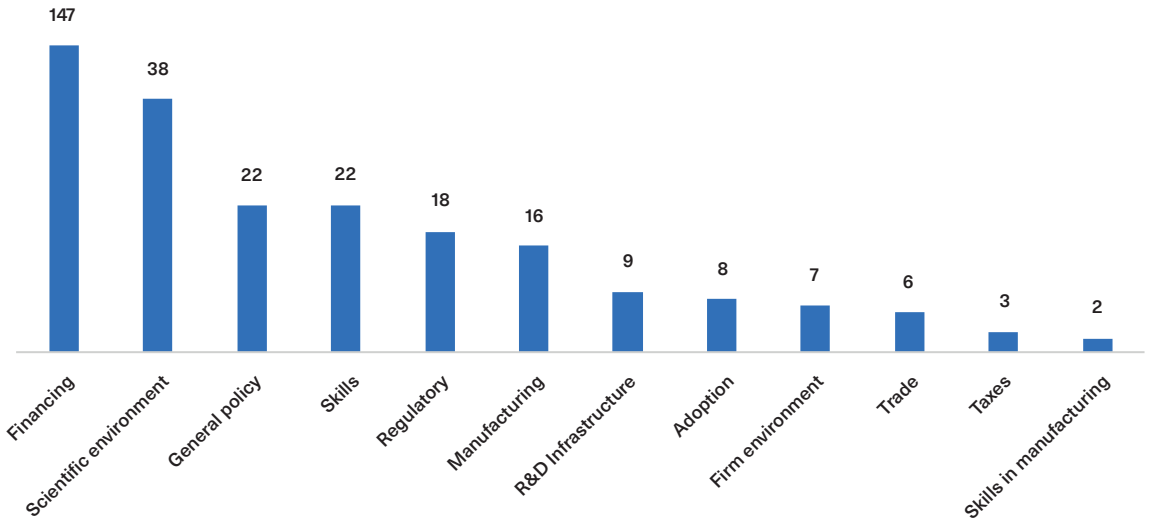

Figure 28: Number of policy recommendations per category that were identified in 30 policy reports that were published between 2015 and 2023. Policy recommendations were categorised

Business environment	Science and R&D	Manufacturing and skills	Regulatory
1. Transparency and reporting of R&D investment, including monitoring pipeline of new drugs produced by UK companies	**4.** Data availability – access, interoperability, linkage	**8.** Targeted support for UK biopharma manufacturing	**10.** Regularly review approaches to pricing and access to innovative drugs
2. Improved and targeted early-stage financial support	**5.** Support for understanding and navigating the data environment	**9.** Up / re-skilling personnel, especially around data science	**11.** Establish a long-term sustained vision for pricing and market access, shared by all stakeholders
3. Support for improving leadership and entrepreneurial skills	**6.** Monitor the integrated care systems' performance in promoting and adopting innovations		**12.** Monitoring the impact of regulatory alignment and divergence on UK performance
	7. Comprehensive review of the mechanisms for supporting innovation adoption and implementation		

Table 5: Recommendations - summary

Business environment

In section 3 we described how the UK biopharma sector's GVA is primarily driven by AstraZeneca and GSK. AstraZeneca and GSK are responsible for the bulk of R&D activity but conduct most of their spending outside the UK, primarily in the USA. Attracting inward investment from foreign biopharma companies, encouraging the relocation of outsourced R&D activities from AstraZeneca and GSK, and promoting the growth of existing UK biopharma firms would all increase the sector's GVA.

The UK has a large number of micro- and small-sized biopharma companies which are R&D active – at the time of our research around three-quarters have measurable R&D output. Micro-sized companies primarily operate at early R&D stages, while large-sized companies are more involved in late-stage clinical activities and drug approval. About a quarter of these companies have entered clinical trials but only around 12% have successfully completed the full development cycle leading to product approval.

Recommendation 1: The lack of systematic data on SME enterprise R&D investment limits analysis that can be done, so industry and government should explore ways of improving transparency and comprehensive reporting.

It could also be useful to monitor the pipelines of smaller companies to identify whether they progress in their drug development cycles and if not, what factors underlying this are.

There has long been concern about the failure to turn promising UK technology start-ups into global players. The UK's biopharma sector has been described as a feeder for the US market. It is essential sufficient growth finance is available to small UK companies, otherwise their early technologies and intellectual property (IP) may be sold prematurely to foreign companies. Our research highlighted the heavy reliance of micro- and small-sized companies on grants, seed funding and angel investors, which provide limited financial support during the initial R&D stages, and venture capital for early preclinical and clinical testing. Once companies begin to generate revenue, private equity deals, corporate investments and public offerings are more likely to be available. Although long-term funders have emerged and the number of venture funds available to small biopharma companies has grown, there is still concern over the availability of lack of finance to pull new innovative products through the system. Two areas of particular concern that have been identified are (1) the ability of smaller companies to engage in concept testing and scale-up; and (2) challenges faced by the data-driven life sciences companies in securing investment. [25,64] Smaller companies face difficulties in accessing financial support to carry out concept testing to industry standards, despite the relatively low costs. This funding gap has not been adequately addressed in recent initiatives.

Recommendation 2a: Improving financial support for scale-up of promising small companies should be a policy priority. This likely to require careful consideration of the wider investment environment (e.g. fiscal and other incentives).

Recommendation 2b: Easily accessible mechanisms to support evidence generation in the earlier stages of the R&D process are essential for improving the flow of potential biopharma through the innovation pipeline. The sums involved are likely to be relatively small and might take the form of grants.

Small data-driven life sciences companies face specific challenges when it comes to securing investment. Biotech investors may feel uncomfortable with the rapidly evolving nature of data technology. Technology investors may be wary of the regulatory complexities related to human health, and their conventional metrics for assessing investment opportunities may not be applicable to slower-moving life sciences companies.

Recommendation 3: Support – perhaps in the form of mentorship and small grants to help develop business models or investment cases – would be useful to help companies articulate their value proposition, develop a clear and concise business model, and demonstrate to investors how they will generate revenue.

Science and R&D

Data infrastructure

The UK needs to increasingly approach biopharma R&D as data science; access to accurate and comprehensive data, and the advanced tools to analyse it, are essential. The abundant data generated by the NHS and other healthcare systems, real-world data sources, and new life science discovery technologies forms the basis for the twenty-first century biopharma sector. Making use of real-world data is still an emerging field, with many unresolved ownership, ethical and privacy challenges. The NHS possesses rich health data, but there have long been difficulties for researchers and life sciences companies in accessing, curating, and sharing this data effectively.

We welcome current initiatives to address these challenges of interoperability and accessibility across and within vertical and horizontal data silos sources in the NHS: the investment to establish secure data environments as the default route for accessing research-ready NHS data, the plans for a federated

data platform to maintain data connectivity, the Data Saves Lives strategy to streamline access and enhance security and transparency.

Recommendation 4a: Industry, regulators and the NHS must speed-up these efforts, and (Recommendation 4b) additionally data users from the life science sector would benefit from linkage between clinical trial data and patient-reported outcome measures, and genomics and phenotypic outcomes.

This requires a commitment by the NHS, government and biopharma to address to make the UK a leader in the breadth and depth of data available for life sciences research and innovation purposes. Achieving this goal will require the collective support and collaboration of policymakers, healthcare providers, professionals, data custodians, the pharmaceutical and life sciences industry, as well as the public and patients.

Start-ups and smaller companies, drug researchers and developers often lack skills in understanding health data access processes and constraints, as well as sources and availability of research data.

Recommendation 5: Current initiatives to provide support for navigating and analysing health and other data through the Medicines Discovery catapult need to be encouraged and strengthened. Government and the NHS also need to investigate the possibility of a centralised information resource on molecular and other biopharma assets, ownership and patent status, and potential collaborating organisations.

The Government has accepted key recommendations by the O'Shaughnessy review, including the need to decrease the approval time for commercial clinical trials and rebuild capacity for approving trials, led by the MHRA and the Health Research Authority (HRA). It also commits to improving the transparency and availability of data regarding commercial clinical trials and has allocated £81 million over three years from the National Institute for Health and Care Research for this purpose. A further £20 million over two years has been pledged to establish clinical trial acceleration networks, focusing initially on infectious disease vaccines, cancer, and dementia. We support these measures, but monitoring their effectiveness on the number of trials started and completed will be important.

The NHS as a context for research and adoption

Significant opportunities for efficient, high-quality research and translation into mainstream healthcare practice exist because of the NHS's cradle to grave health records on the entire UK population and its status as a single payer. However, there are widespread concerns about its current capacity for engaging in research. Operational pressures and funding constraints mean there is little time for implementation of innovations, especially where healthcare processes need to be adapted and new learning is needed to ensure the innovation is correctly implemented.

More broadly, the NHS remains a complex and fragmented environment for adopting healthcare innovations. The NHS needs to be far more efficient at adopting, implementing and diffusing new treatments and technologies. The introduction of Integrated Care Systems (ICS) in 2022 and continued evolution of the AHSNs are potentially a step forward. The Hewitt review of ICS [66], reporting in April 2023, reiterated the role of Academic Health Science Networks (AHSNs) in helping to stimulate and introduce innovations across local healthcare systems. We support the review's emphasis on the need for careful alignment of AHSNs with local ICS priorities to spread and adopt innovation and best practice efficiently. As the ICS begin to mature, the challenges in implementing and embedding innovations which result from silo thinking – both organisational and financial – should begin to diminish. The Hewitt review noted the possibility for an enhanced role for the Care Quality Commission (CQC) in capturing the innovation efforts of ICSs as a tool for development and improvement.

Recommendation 6: Ensure ICS have consistent and coherent approaches to the adoption of biopharma innovations and develop metrics for assessing ICS maturity and performance in relation to the promotion and introduction of appropriate innovations.

The availability of data is an essential component of this process and ICSs will need to ensure data collection systems are timely, high-quality and transparent

Fifteen years ago, Policy Exchange estimated that around twelve times more public funding is spent by the UK on the creation of health technology innovations than on supporting their adoption and implementation. [67] There are no recent estimates of the value of the public investment in this direction, but despite significant improvements in the infrastructure for encouraging adoption and spread such as the AHSNs, the balance of support still favours the early stages of innovation development.

Recommendation 7: Government needs to commission an up-to-date comprehensive review of all the mechanisms for supporting adoption and implementation to ensure that they are as effective as possible and still relevant to research and industry needs.

Manufacturing and skills

The re-shoring of manufacturing activity in the UK's healthcare sector should be driven by broader strategic considerations rather than solely focusing on increasing domestic production. The British Generic Manufacturers Association (BGMA) emphasizes the need to enhance the overall resilience of the generic and biosimilar medicines supply chain while maximizing the industry's economic contribution to the UK. [71] This would partly be based on a categorisation of critical drugs, but according to the BGMA, the supply of active pharmaceutical ingredients (API) and raw materials is a more significant threat to supply chain resilience than the location of drug manufacturing sites.

The BGMA has put forward various incentives to improve UK manufacturing capacity, such as capital grants for flexible advanced manufacturing facilities. Establishing common international quality standards for manufacturing is also seen as a way of ensuring fair competition between countries. In recent years the UK government has started to offer funding for innovative life science manufacturing with the Medicines and Diagnostics Manufacturing Transformation Fund (MDMTF) pilot programme which launched in April 2021 and the recently introduced Life Sciences Innovative Manufacturing Fund (LSIMF), with a small amount government funding (£17 million) matched by additional private investment of £260 million. [72]

Recommendation 8: There should be targeted support for UK manufacturing, focused on innovative manufacturing techniques, and the manufacturing of critical medicines and APIs and advanced therapies. This should be accompanied by better evidence on where such support should be targeted and the likely impact of different measures.

While there was initial uncertainty about the impact of the UK's exit from the EU on talent recruitment, this concern seems to have decreased. There has been progress in addressing skill shortages, but there are still certain disciplines where shortages persist, notably – given the increasing role of data science in the biopharma sector – these tend to be related to data and digital skills. [55] Maintaining a focus on STEM skills within the education system and ensuring there is access to training to develop the data science skills required within biopharma remain essential.

Recommendation 9: Industry has an important role to play in re- and upskilling its workforce in this regard, and in promoting the diverse and viable career pathways within the sector. This includes improving the leadership and entrepreneurial skills needed to build and scale biopharma businesses. [2]

Regulatory

The methods and processes used by the National Institute for Health and Care Excellence (NICE) to appraise new drugs and treatments have evolved and there is now more flexibility and pragmatism in its approach. These include acceptance of higher uncertainty in evidence generation in rare diseases and complex therapies, support for the use of more comprehensive evidence, including real-world evidence and patient experience of care, and greater consideration of the broader healthcare system costs.

Industry continues to raise concerns about NICE's decision not to change the discount rate it uses in appraisals and the potential impact this has on the valuation of new drugs. Others have argued that further research is needed on the appropriate theoretical and empirical basis for discounting practice. [68] NICE is a leader in the evaluation of new health technologies and as such it helps to signal to global investors and biopharma companies the UK's commitment to innovation.

Recommendation 10: It is essential that NICE's approach to appraisal is regularly and independently reviewed against the changing context of public expectations, the realpolitik of government resource allocation, and the evolution of technological innovation and breakthroughs in science.

The Voluntary Pricing and Access Scheme (VPAS) agreement between the government and the pharmaceutical industry aims to balance the cost to NHS of drugs and fair returns to the biopharma industry. The decision to raise the rate from 15% to 26.5% has led to backlash from the biopharma industry, which argues that the new rate is far higher than comparable countries. The ABPI is calling for a new scheme and has proposed that pharmaceutical companies pay an extra 1.5% of UK sales into an investment fund to improve NHS clinical trial capacity, expand the UK's genomics research capacity, and support a medicines equity partnership to address local challenges to the adoption of new drugs. [69] The British Generic Manufacturers Association (BGMA) has argued for exemptions from the VPAS rebate for biosimilar drugs and branded generics where branding is a regulatory requirement. The BGMA is currently involved in a judicial review to challenge the decision taken by the Secretary of State not to include it in discussion over the form of a post-2023 VPAS. The BioIndustry Association (BIA) has also criticised the scheme. Negotiations between government and the industry over approaches to drug pricing in the UK are continuing at the time of writing.

Recommendation 11: We reiterate the importance of all parties establishing a long-term sustained vision for pricing and market access, shared between government, NHS, NICE, the biopharma industry and other key stakeholders. This needs to acknowledge the importance of balancing access and affordability, with support to ensure the competitiveness and sustainability of the UK's biopharma sector.

Following Brexit, the MHRA became an independent regulatory agency. Our research on its first year of independent operation suggested there had been some delays in authorising certain novel medicines, although the reasons were unclear. Furthermore, the available data suggested the at least 70% of new drugs were authorised through a temporarily introduced EU reliance mechanism. In this context, the government announced that from 2024 onwards the MHRA would be able to follow other trusted regulators, including the EMA, FDA and its Japanese counterpart, to free up time and resources and enable it to focus on more innovative products.

We welcome this move towards regulatory harmonisation and reduction in unnecessary regulatory burden, but it will be important to ensure that the full impact of regulatory policies on authorisation of biopharmaceutical innovations and access for patients continues to be monitored.

Recommendation 12a: Monitor the performance of the UK in authorising innovative new drugs. Comparison with the only other independent European regulatory body Swissmedic might be useful to understand the functioning and efficacy of their regulatory system and the lessons for UK as an independent European country.

In April 2023, the European Commission published its proposed revisions to the basic pharmaceutical legislation as a part of its overall of European biopharma strategy. Objectives include new incentives to promote wider access to medicines across EU countries, address unmet medical needs, facilitate early availability of generics and biosimilars, and simplify market authorizations. The plans also aim to create a favourable regulatory environment for new and repurposed drugs by moving from a 'one-size-fits-all' to a more flexible framework for regulatory protection and IP rights. [70]

There is no clear timeline for adoption of the measures and given the 2024 European elections the negotiation process may well continue well into the next mandate. Industry groups have expressed concerns that the changes to incentives will undermine innovation without guaranteeing better access for patients.

Recommendation 12b: Government and the biopharma industry will need to monitor progress towards more flexible EU regulatory pathways on their impact for the UK's attractiveness for biopharma R&D, drug trials and product launches.

One area where the UK should ensure it remains competitive is in the regulation of data and data driven life science companies and products, including use of real-world data and responsible data use, assessment of more complex drug/device combination products, and IP protection of data-driven life science products.

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Appendix
Methodology

Biopharma ecosystem database

A firm-level database was created to help characterise the biopharma ecosystem. This consists of all national and international companies that are involved or supporting the development, manufacture or supply of medicines in the UK, including pharmaceuticals and biopharmaceuticals. It doesn't include the emerging data science sector supporting biopharma R&D.

The database was created by combining two datasets:

- the bioscience and health technology sector statistics 2019 'Biopharma core' dataset provided by the Office for Life Sciences (OLS)
- the GMDP database by the Medicines and Healthcare Products Regulatory Agency (MHRA).

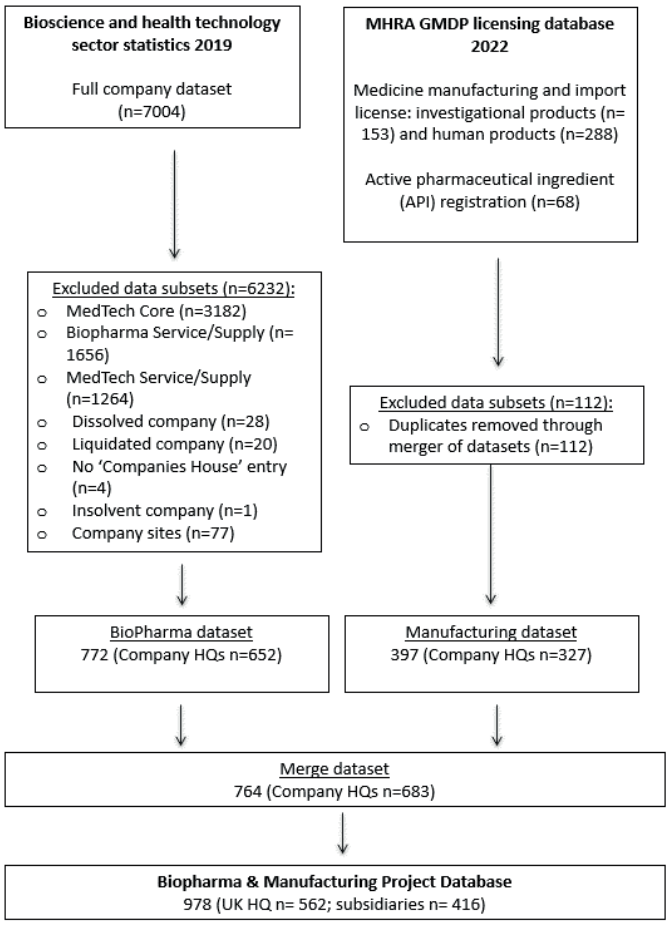

Figure 1: Flow chart of the BioPharma Ecosystem project database combining the data of two datasets.

The merged firm-level database was cleaned by (1) using only the group account for all UK head-quartered companies, (2) using single company accounts for all companies and subsidiaries of companies with overseas headquarters, (3) removing companies with Companies House 'Overseas' registrations, and (4) removing companies without available economic information or large companies without a life science focus (e.g. British American Tobacco) (Figure 29).

This approach was able to capture a wider range of companies than the current ONS industry classification for the "manufacture of pharmaceutical products" (SIC 21). Of the 977 companies in our ecosystem database, approximately 20% had SIC21 annotated as their primary SIC code.

The database is broken down into five segments:

- Biopharma: 591 businesses involved in developing and/or producing pharmaceutical products.
- Manufacturing: 141 businesses with import and manufacturing license for medicines in the UK with registered activity of medicines manufacturing.
- Supply: 105 businesses with import and manufacturing license for medicines in the UK with registered activity of import, quality control and packaging.
- Biopharma and manufacturing: 82 businesses involved in developing and/or producing their own pharmaceutical products and with registered activity of medicines manufacturing.
- Biopharma and supply: 58 businesses involved in developing and/or producing their own pharmaceutical products and with registered activity of import, quality control and packaging.

The database contains firm-level data on financial performance, employment, productivity / contribution to the UK economy (gross value added and gross value added per employee), capital market financing, enterprise R&D spending, manufacturing sites and capabilities, as well as R&D output including patents.

The analysis spans 2016 to 2021 and nominal values are reported, i.e. they have not been adjusted for inflation or economic multipliers.

Other data

Financial and economic variables were extracted on a firm level from Bureau van Dijk and aggregated for analysis (Table 1). It should be noted that financial data was not available from all companies, with more limited data on younger and smaller companies as highlighted previously for Bureau van Dijk databases. 73

Direct GVA was calculated with the formula GVA = employee costs + operating profit (EBIT) + depreciation + amortisation, which is consistent with the national accounting methods used by the ONS and other reports. 8 The estimated GVA was consistently higher than the ONS reported figures, which could be explained by the different pool of companies that were considered in this database including biopharma companies and manufacturing companies.

Dataset	Sources	Variables
Biopharma ecosystem	1. BEIS- Office for Life Sciences bioscience and health technology sector statistics 2019 (Biopharma core subset) 2. GMDP MHRA database (Manufacturing and Import authorisations for human use & API registrations; data extracted at the end of 2022)	• Company name • Geography/postcodes • Manufacturing capabilities • Supply capabilities
Headquarters *	ORBIS Intellectual Property/ ORBIS EUROPE/ FAME (Bureau van Dijk)	• R&D headquarter location • Domestic headquarter location (if applicable) • Investment parent (if applicable) • Geographic profile
Financial data **	ORBIS Intellectual Property/ ORBIS EUROPE/ FAME (Bureau van Dijk)	• Turnover • Profit • Employment • Business R&D investment • GVA components (employee costs + operating profit/EBIT + depreciation + amortisation)
Private capital market financing **	Pitchbook	• Type of investment • Number of investments • Size of investment • Stage of business
Patent data/ R&D location **	ORBIS Intellectual Property (Bureau van Dijk)	• Patent categorization • Patent inventor location • Number of citations
R&D output *	1. Clarivate Web of Science, Elsevier Scopus 2. Clinicaltrials.gov, EudraCT, ISRCTN registry 3. ORBIS Intellectual Property (Bureau van Dijk) 4. MHRA, EMA & FDA	• Publications (company listed in affiliations) • Patents • Clinical trials • Marketing Authorisations

Table 1: Overview of datasets and variables of the UK BioPharma Ecosystem project database

R&D location / patent inventor location

The location of the patent inventor was used as a surrogate for the location of the R&D for all companies in the database; when R&D expenditure was reported, it was allocated to R&D locations as determined by the patent analysis. The analysis covered patent families (groups of patents associated with the same innovation and submitted in more than one country) that were filed between 2016 and 2021.

The dataset comprised a breakdown of patenting activity for each company that was aggregated at country level to obtain information on inward, outward, and home R&D activity. R&D location / patent inventor location was also used to estimate the home, inward, and outward investment in monetary terms. For this calculation, global R&D investment figures by company headquarters were divided and R&D expenses were allocated to geographic distribution of patent inventors as outlined above. This data was not available for all companies; the estimate is based on data from 227 of 652 companies in the database (35%).

EU Scoreboard

The EU R&D Investment Scoreboard is published annually and provides an annual list of the companies with the highest enterprise R&D spending worldwide (top 2500 companies) and in the EU (top 1000 companies). It contains company count and financial performance data. We combined all EU Scoreboard datasets between 2014 and 2020 and used it to benchmark and observe the development over time of UK headquartered biopharma companies compared to other countries and their biopharma industry on R&D investment, sales, employment, and patenting activity. The methodology was consistent in the years 2014-2020, before the methodology was changed amid Brexit.

Clinical trial data

NIHR Innovation Observatory Scan Medicine database was used to collect data on clinical trial sites and their location of all publicly registered clinical trials (phase 1-3) that were initiated, recruiting or completed during 2017 and 2021.

Private capital investment

Pitchbook database was used to extract all data related to international private capital investments in two sectors: biotechnology and pharmaceuticals. These sectors are defined and managed by Pitchbook. The biotechnology sector is defined as companies engaged in research, development, and production of biotechnology. Includes embryology, genetics, cell biology, molecular biology, and biochemistry, among other activities. In this category, 44% of companies are also listed as performing 'drug discovery', i.e. researchers and developers of new drugs, including the identification, screening, and efficacy testing of drug candidates.

The pharmaceutical sector is defined as manufacturers and distributors of established drugs / pharmaceuticals, including any large drug company that primarily manufactures medicines (they may also be engaged in drug research and development). In this category, 33% of companies are also listed as performing 'drug discovery', i.e. researchers and developers of new drugs, including the identification, screening and efficacy testing of drug candidates.

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