Driving Global Competitiveness of the UK’s Life Sciences Ecosystem

For the benefit of UK patients, the economy and the NHS
Foreword

Erik Nordkamp, Managing Director, Pfizer UK

Today every one of the top 20 global pharmaceutical firms has a presence in the UK, investing billions of pounds in research and development, creating tens of thousands of jobs, making a significant contribution to the health and wealth of the UK.

Pfizer commissioned this analysis to inform our response to the Government’s Industrial Strategy consultation as it looks to strengthen a globally competitive UK life sciences sector. As a global company we see many emerging and developed economies increasingly grow and strengthen their medical R&D capabilities. Some of those countries are benchmarked in this analysis – US, Singapore and Switzerland.

This analysis tells us that to have a competitive life sciences sector a holistic ecosystem is needed. The analysis finds that the UK is world leading on the two most important factors of that ecosystem – a strong science and academic base, and a highly skilled and highly productive workforce in life sciences. The area where the UK is significantly trailing behind its competitors on attracting a share of global R&D, especially in high value, late stage R&D, is in patient access to the best medical treatments. This analysis tells us that it is the third most important factor in making investment decisions and the UK trails significantly behind.

The encouraging conclusion of this analysis is that reducing this access gap could lead to an estimated additional £705m in GVA per year and 4000 jobs, many of which would be high skilled jobs in the UK life sciences sector; generating an estimated additional £244m in tax (which benefits the NHS); and giving UK patients better access to the latest medical innovations.

This is a prize worth aspiring to and we as industry are committed to working with the Government and the NHS to make sure the UK remains a global leader in the development and use of new medical technologies.
Foreword

Jo Pisani, Partner, PwC Strategy&

In the UK we have a vibrant pharmaceutical and life sciences sector which makes a significant contribution to our overall health and wealth – the UK is responsible for discovering and developing many of the world’s medicines, and the pharmaceutical sector supports £15.7bn in GVA, and 312,000 jobs, employing 71,000 people directly and supporting a further 241,000 jobs through the supply chain and economy.

Our analysis shows that UK competitiveness requires top performance across several factors and through interviews with sector leaders we found: academic & leading edge science, workforce & skills and access to medicine are the most important of these.

A benchmarking exercise examining the performance of France, Germany, Japan, Singapore, Switzerland, the UK and US, demonstrated UK excellence in academic & leading edge science and workforce & skills. However, a significant lag is seen in patient access to new medicines.

In fact UK patients accessed significantly less new medicines in the first year of launch when compared to patients with the same diseases in the benchmark countries. This trend was consistent in products with and without NICE recommendations and across disease areas.

If access were improved we estimate that 4000 new UK jobs could be created by 2021 (many in R&D), and £705m in Gross Value Added (GVA) realised each year thereafter, in addition to health and welfare benefits and further consequential increases in commercial and manufacturing jobs.

Of course, improving access is complex, but there is opportunity for the UK to enhance its competitive edge to benefit patients, the NHS, and the economy. By agreeing a shared aspiration to improve patient uptake of new medicines, a range of approaches can be explored. These could include the adoption of innovative pricing models, implementation of the Accelerated Access Review, or multi-year NHS budgets. Achieving this will require greater collaboration across industry, the NHS, Government and patients.

We thank all the contributors to this report and look forward to working with you all to drive UK competitiveness in life sciences and UK health and wealth, into the future.
Pfizer Ltd commissioned analysts from PricewaterhouseCoopers LLP "PwC" to develop the methodology and perform the analysis detailed in this report. This analysis has been prepared only for Pfizer Ltd and solely for the purpose and on the terms agreed with Pfizer Ltd in our agreement dated 10th January. PwC accept no liability (including for negligence) to anyone else in connection with this analysis. Pfizer Ltd has been involved in the scope and methodologies of the analysis and had final editorial control of the report.
Executive summary

Key findings

- The UK Government seeks to become a globally-unique and internationally competitive life sciences ecosystem that delivers health and wealth and supports NHS transformation.

- This analysis revealed that workforce & skills, academic & leading edge science and access to medicines are the three most important ecosystem factors in achieving this vision.

- The UK is globally competitive in academic & leading edge science and workforce & skills, it is in-line with other leading countries in fiscal incentives and clinical trials infrastructure, but lagging behind significantly in access to medicines.

- This analysis found that UK patients have significantly lower uptake of new medicines (up to 75% by volume per capita) in their first year of launch. It then takes on average almost two years to catch up with the next lowest uptake country. Even with NICE approval and ‘novel’ designation UK patients have up to 64% lower uptake (by volume per capita).

- If the UK reduces this “access gap” in new medicines available to patients it could better support growth in the life sciences ecosystem: 4000 new jobs could be created by 2021 and £705m in Gross Value Added (GVA) realised each year. It could also stimulate healthcare improvements for patients, support NHS transformation and UK R&D.

- As well as generating job and economic value, this would revise the current situation where the UK has a strong record in developing some of the world’s cutting edge medicines but patients in the UK have significantly less access to new medicines than in other countries with strong life science hubs.

- Looking forwards, NHS challenges, the need for cost containment and the unique strengths of the NHS, such as universal healthcare free at the point of delivery, must be recognised. This analysis has identified opportunities to collaborate across the health system and industry to improve access to new medicines and support cost containment through:
  - Agreeing an aspiration to improve patient uptake of new medicines (e.g. bringing the UK broadly in line with comparable peers based on GDP per capita, population and health system dynamics such as France and Germany, by 2021), and
  - Exploring a range of approaches such as the adoption of innovative pricing models, that support both patient access to new medicines and NHS cost containment.

- This report aims to provide a useful basis for further discussions on how this successful life sciences sector can continue to drive UK innovation, health and economic benefit, into the future.
What is the level of innovation and productivity in the UK’s life sciences sector?

The UK has a strong academic base, leading edge scientific institutes, an active investment market and the NHS. This creates a vibrant pharmaceutical sector, with high productivity, jobs and economic value (£9.6bn in direct GVA and 71,000 in direct employment).

The UK Government’s ambition is to become a globally-unique and internationally competitive life sciences ecosystem that delivers health and wealth and supports NHS transformation.

The pharmaceutical sector supported £9.6bn in direct Gross Value Added (GVA) in 2015, and a further £6.1bn through the supply chain and in the economy. It employed 71,000 people in the UK and supported a further 241,000 jobs in the economy, and contributed £4.1bn in tax payments to the UK\(^1\), of which ~20% flows to the NHS\(^2\). Pharmaceutical manufacturing has one of the UK’s highest levels of productivity. The UK’s pharmaceutical manufacturing sector boasts 40% higher productivity levels than Germany and 80% higher than France\(^3\) and the UK has the largest pipeline of biotech products in Europe\(^3\).

Yet the UK cannot be complacent. Global competition from emerging markets is increasing in highly skilled sectors, the US (the largest global market) is indicating a shift towards protectionist policies and the UK itself faces huge uncertainties following the 2016 Brexit referendum. Any one of these situations alone would pose challenges, but the combination means there has never been a more critical time to focus on competitiveness. This is the opportunity for the UK to enhance its competitive edge to benefit patients, the NHS and the UK economy.

What were the most important factors driving investment in innovation?

To drive international competitiveness of a life sciences ecosystem the most important factors are workforce & skills, academic & leading edge science and patient access to medicines.

To attract life sciences innovation the UK requires an internationally competitive ecosystem. In any country a life sciences ecosystem is based on complex interactions between several factors, which create the overall attractiveness of the country. Nonetheless there are certain factors that are more important to life science activities in early and late stage R&D, manufacturing and commercial activities.

R&D activity is driven by science, yet other factors matter too when making investment decisions. For pharmaceutical companies, in early stage R&D academic & leading edge science (29% of votes) and workforce & skills (15%) are critical, with patient access to medicine and clinical trials infrastructure joint third (12%). Stakeholders reported unique science overrides other factors. In Late stage R&D, the most important factors are clinical trials infrastructure (23% of votes), along with patient access to medicines (19%) and academic & leading edge science (19%).

What was the analysis methodology?

This analysis, conducted by PwC Strategy&, explores the strength of the UK life sciences ecosystem and the opportunity for a stronger life sciences sector that benefits the economy, the NHS and patients in the UK.

In conducting this analysis PwC Strategy& have: performed a literature review of 19 reports to determine 12 ecosystem factors that impact innovation, selected 6 countries to benchmark UK performance against and conducted 33 stakeholder interviews\(^4\). The interviews have sought to determine: the relative importance of different ecosystem factors on innovation and how access to medicines compares, UK performance against benchmark countries on each ecosystem factor and the impact of an improved access scenario on innovation i.e. R&D (split by early and late stage), Manufacturing (advanced therapy medicinal products) and Commercial (specialist functions).
Clinical trial activity and resulting investment is highly mobile and competitive. Stakeholders reported there is no guarantee for the UK as a future destination for large scale Phase III trials. Running global standard trials and knowing patients can access drugs after the trial are of high importance to pharmaceutical companies. There are economic benefits to the NHS of these trials since treatment and drug costs are borne by the trial sponsor.

For small biotech companies, venture capital firms, academics and others, in early stage R&D they also prioritised academic & leading edge science (26% of votes), but gave a greater share of their votes than pharmaceutical companies to funding & investment (14% of votes) and international and regional collaborations (9% of votes). These were voted in joint third place alongside access and clinical trials infrastructure. In late stage R&D, similarly they prioritised academic and leading edge science but also digital & data as most important (18% of votes each) as small biotech firms look to more easily work with hospitals to identify patient cohorts.

For advanced therapy medicinal products manufacturing (which includes cell and gene therapies) the most important factors are workforce & skills (36% of votes), fiscal incentives (30%) and infrastructure (11%). Stakeholders reported manufacturing of advanced therapies requires skills found globally, requiring the ability to attract top global talent. Access to medicines was referenced as the fourth (9%) most important factor, particularly in areas where the patient’s own cells are used. Here there are benefits to patients being near to manufacturing and R&D sites.

Whilst for commercial activities, workforce & skills (30% of votes), fiscal incentives (18%) and infrastructure (15%) are the most important factors. Specialist commercial teams travel between global HQ and other offices regularly and rely on good infrastructure e.g. air and rail hubs.

How is the UK performing compared with other global life science hubs?

The UK is a leader in science and skills. It could capitalise on the NHS to improve UK life sciences competitiveness in digital & data and clinical trials infrastructure, and on the City’s financial standing to further funding & investment. The UK trails other markets significantly in patient access to medicines; improving access would enhance UK competitiveness for investments in life sciences R&D.

Benchmarking the UK against France, Germany, Japan, Singapore, Switzerland, and the US, reveals areas of current leadership, potential excellence and performance gaps. These countries were chosen based on their reputations as leading life sciences markets, for a range of reasons e.g. the US is the largest pharmaceutical market by value, Switzerland is well known for its tax incentives and large pharmaceutical company presence, whereas Singapore is a popular destination for clinical trials and acts as a gateway to Asia for life sciences companies.

Each country’s health system has different levers available to support innovation and contain costs (e.g. health technology assessments, medicines budget capping, co-payment, delayed access etc.). The dynamics and historical context of each country impacts competitiveness across factors. Analysis of UK performance demonstrates:

Current leadership: The UK has world leading capabilities and institutions in academic & leading edge science (1st US, 2nd UK, 3rd Switzerland) and workforce & skills (1st Switzerland, 2nd UK, 3rd France). Maintaining and if possible expanding this leadership is critical to innovation in early stage R&D, particularly in the context of challenges and opportunities following the Brexit referendum.
Potential excellence: The UK is competitive, but further away from 'best-in-class' countries on international & regional collaborations, and presence of pharmaceutical companies (distant third to US and Switzerland, two highly competitive markets). On funding & investment, public funding by the UK trails all other markets (particularly Singapore and the US) which brings the average rating down. The UK could leverage the financial capabilities of The City and venture capital (VC) market to develop end-to-end funding & investment solutions for biotechs. On digital & data and clinical trials infrastructure, the UK sits within a cluster of other markets like France and Germany. However, the UK has a unique asset in the NHS as a single payer providing universal access, with the potential to join up data and support innovation and research to improve patient care. The UK could become a leading destination for real world evidence (RWE) generation and clinical trials. On the latter, stakeholders raised concerns about UK use of the Standard of Care therapies, which deters companies from conducting UK trials, particularly in oncology. In addition to the ethical challenge posed if patients are recruited onto trials but further access to the drug is not offered in the UK.

Performance gaps: There is only one factor where the UK is significantly trailing other comparable countries: patient access to medicines. The data show the UK trails others countries on access to medicines. This analysis found that access to medicines is an important factor in life sciences investment decisions including in R&D, manufacturing.
What is the UK access gap?

UK patients experience significantly lower uptake of new medicines; up to 75% less by volume per capita in their first year of launch and it takes on average almost two years to catch up with the next lowest uptake country. Even with NICE approval and ‘novel’ designation UK patients experience up to 64% lower uptake (by volume per capita in the first year after launch). The gap is seen across multiple disease areas.

This analysis has found up to 75% lower uptake of new medicines for patients in the UK, compared to patients in France, Germany, Japan, Switzerland and the US.

Figure 2: Uptake of 76 patented drugs launched 2011 – 2016 by volume pmp, first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy & analysis

UK access is low and slow, it takes on average almost two years to catch up with the next lowest uptake country.

The difference between the UK and the average across benchmarked countries ranges from 49% for oncology to 89% in hepatitis C. Although this report has not evaluated the health impact of low access on patients across countries, the differential in access and the slow uptake suggests patients are not receiving the latest therapies, or where they do it is following significant delays.

For products that have been awarded a novel designation in the US (due to being categorised as “among the more innovative products that often help advance clinical care to another level”)\(^x\). UK uptake is up to 67% lower than the average of other countries. The data also show that low uptake is not necessarily caused by NICE’s assessment criteria. A similar uptake differential (up to 64%) is seen even where there is a NICE recommendation.

Some pharmaceutical companies recognised positive features of the NICE assessment processes such as robustness, transparency and predictability but found the narrow focus on cost per QALY inflexible and in need of reform when assessing some specialist therapies. However companies experienced barriers to uptake in the NHS following NICE approval which included: fragmented negotiations with over 200 clinical commissioning groups and NHS England decision-makers and the fact that the NICE 90 day NHS mandate is not always upheld. At the time of publication a budget impact test is planned. The test will enable NHSE to opt out of the 90 day mandate and introduce medicines costing over £20m (in one of the first three years of launch) in a phased way over three years\(^x\).

What are the economic benefits of reducing the access gap?

Closing the access gap between the UK patients and patients in similar countries could strengthen the sciences ecosystem, particularly in R&D, and stimulate healthcare improvements for patients and NHS transformation. Through additional R&D alone, 4000 new jobs could be created by 2021 and £705m in Gross Value Added (GVA) realised each year.

Access is important in driving innovation and investment, especially in clinical trials. This report estimates how an improved access environment could impact the level of innovation in the UK life science ecosystem. Analysis shows that closing the access gap could increase the level of R&D in the UK creating positive benefits for the life sciences ecosystem, economy, NHS and patients.
In this analysis, an increased access scenario was described to stakeholders as: pharmaceutical spending is increased or there is a greater share for innovative drugs, an expanded model of accelerated access is applied (similar to FDA Breakthrough Therapy in the US), NICE approval is accelerated to an earlier R&D stage (Ph. II), reimbursement is linked to Real World Evidence (RWE) and the UK becomes a leader in innovative pricing and rewards innovation. Stakeholders were asked what impact this would be likely to have on investment in R&D and jobs.

This analysis found that increasing access could create an additional 4000 UK jobs by 2021, of which 1900 would be a direct increase in life sciences R&D jobs and the remainder would occur through multiplier effects in the supply chain for example in Contract Research Organisations (CROs). At a steady state this would boost UK GVA by £705m each year. This additional activity could result in an increase in tax payments of £244m. As around 20% of public sector expenditure goes towards the NHS, a large proportion of this would flow back into UK health care. Further, widening access to innovative medicines could have many more benefits, which have not been quantified in this report, such as health benefits and welfare effects from reduced absences from work and boosting the economy.

Although this analysis focuses upon the estimated impact in terms of R&D, a number of organisations also outlined an impact on non-R&D functions, however this was a smaller sample and therefore not included.

Many companies discussed the impact of Brexit and the potential challenges and opportunities this creates for innovation. Given these uncertainties, improving access and uptake of new medicines and stimulating the UK life sciences ecosystem, becomes even more critical going forward.

How do we close the access gap in order to maintain an internationally competitive life sciences ecosystem that delivers health and wealth for the UK?

Recognising the strengths of the NHS as well as its cost containment challenges is essential to improving patient access to new medicines and supporting NHS transformation. Government, the NHS and industry jointly aspiring to and collaborating on improving patient access to new medicines is needed in order to retain life sciences investments in the UK in a globally competitive environment.

The UK aims to become a globally-unique and internationally competitive life sciences ecosystem that delivers health and wealth and supports NHS transformation. To achieve this, a competitive ecosystem is needed across all factors. It is important to maintain leadership in areas such as science and skills (particularly in the context of the challenges and opportunities created by Brexit), to become more competitive on clinical trials infrastructure, digital & data (e.g. RWE) and funding & investment, and, especially, to improve access to new medicines.

Narrowing the access gap can drive UK life sciences competitiveness, boost UK R&D jobs and stimulate UK science, skills and clinical trial activities. It could revise the current situation where the UK has a strong record of researching and developing innovative medicines, but UK patients access significantly fewer new medicines compared with other leading countries.

This report recognises the unique strengths of the NHS, the broader context of NHS transformation challenges, including the need for cost containment. New approaches involving the Government, NHS and industry are needed. Industry is currently a partner in managing healthcare expenditure through a voluntary agreement with the Government to cap the total new medicines bill (which offers a rebate on expenditure exceeding it), yet the benefits are not currently felt directly by the NHS medicines budget.
This report highlights an opportunity for the UK life sciences and health sectors to agree an aspiration to reduce the access gap. For example, that patient access to new medicines in the UK is broadly in line with comparable peers based on GDP per capita, population and health system dynamics (such as France and Germany), by 2021. This shared aspiration by senior Ministers, industry and the NHS leadership to prioritise access to the latest pharmaceutical innovations based on patient need, can be delivered through collaboration.

Stakeholders also called for a wide-ranging new approach to access and uptake that goes beyond current UK plans to implement the Accelerated Access Review. The following approaches which have been suggested by stakeholders and seen in other leading markets could be explored:

- **Implementation of innovative pricing models.** In these models a company is paid by the NHS only when the drug or therapy achieves a specified outcome e.g. a clinical response to the therapy, improved adherence, or a reduction in A&E admissions. These models enable the health system to deliver outcomes and achieve greater cost effectiveness;

- **Multi-year budgets** would enable the NHS to invest in a therapy in year one, when a saving may only be delivered in years two or three;

- **Better integration** across the budgets and organisations would allow net savings to be realised, where currently perverse incentives can lead to greater overall NHS spending as additional spend is required in one budget e.g. spend on new therapies, but a more significant saving is realised elsewhere.

- In some cases health system stakeholders from the Department of Health, NICE and NHS England could work together to develop a better overall commercial arrangement, and enable the NHS to transition services in consultation with health care professionals and patients where new innovation could offer savings;
Chapter 1 – What are the most important factors driving investment in innovation?
To drive UK life science global competitiveness the most important factors are workforce & skills, academic & leading edge science and medicines access and uptake, according to pharmaceutical companies and life sciences stakeholders.

1.1 Methodology

In order to evaluate UK performance in life sciences innovation, twelve overarching ecosystem factors were determined from a literature review of nineteen publications. The factors were chosen based on their importance and coverage in key publications, with the aim to cover the ecosystem as a whole, ranging from drivers of scientific productivity to economic attractiveness. The twelve ecosystem factors are listed below, grouped into three primary categories:

In order to determine the most important ecosystem factors in driving investment in innovation, interviews were conducted with stakeholders from across the pharmaceutical and Life Sciences sector, with a focus on the companies that make up the majority of investment in innovation in the UK.

Stakeholders were asked:

1. Which three ecosystem factors (out of the twelve provided) are most important when deciding where to conduct each of the following above-country activities e.g. R&D, advanced therapy medicinal products manufacturing, commercial functions?

Figure 3: 33 interview respondents, include industry associations, biocluster hubs and health system experts

Source: PwC Strategy& interviews, Feb. 2017

Figure 4: Twelve factors that impact the life sciences innovation ecosystem

<table>
<thead>
<tr>
<th>Science, Innovation &amp; Scale</th>
<th>Economic &amp; Political Environment</th>
<th>Health &amp; Commercial</th>
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<tbody>
<tr>
<td>Workforce &amp; skills</td>
<td>Funding &amp; venture capital (VC) investment</td>
<td>Clinical trials infrastructure</td>
</tr>
<tr>
<td>Academic &amp; leading edge science</td>
<td>Fiscal incentives</td>
<td>Digital &amp; data (including Real World Evidence, RWE)</td>
</tr>
<tr>
<td>Large Pharmaceutical industry presence</td>
<td>Trade &amp; export conditions</td>
<td>Patient access to medicines (including regulatory approval, reimbursement, and physician prescribing)</td>
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<tr>
<td>International &amp; regional collaborations</td>
<td>Soft factors (language, culture)</td>
<td></td>
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<td></td>
<td>Infrastructure (rail and air hubs)</td>
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Sources: PwC Strategy& analysis and literature review, see Appendix A

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1 Publications used in the literature review can be found listed in Appendix A
2 Industry organisations were targeted based on size and representation across pharmaceuticals, biotech and of stages in the value chain. Organisations interviewed can be found in Appendix B
3 Stakeholders such as academics, research charities, venture capital (VC) firms and small biotechs were asked about R&D only Q1: Which three ecosystem factors are most important in stimulating R&D in the UK? Some respondents gave either two or four most important factors, resulting in differences in the number of votes for the following figures
2. How important is the access environment relative to your prioritised factors? What is it specifically about the access environment that is most important (if applicable) and how does it impact your activities?

3. Which part of access is most challenging in the UK (e.g. regulatory Health Technology Assessment (HTA), commissioning, healthcare professional (HCP) uptake)?

1.2 Factor importance: overview

In any country a life sciences ecosystem is based on complex interactions between several factors, which create an overall attractiveness. Despite this certain factors are more important to innovation activities (e.g. R&D, manufacturing and commercial functions). This report looks specifically at manufacturing of advanced therapy medicinal products such as cell and gene therapy, and specialist ‘above-country’ commercial functions that have regional or global reach, such as regulatory or analytical expertise.

1.2.1 Most important factors overall

Figure 5: Most important factors to innovation overall. N shows the total number of votes, each stakeholder was asked to vote for three factors per type of innovation area

N = 254

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Overall the most important factors across all types of innovation activities (R&D, advanced therapy medicinal products manufacturing, specialist ‘above-country’ commercial functions) are workforce & skills, academic & leading edge science, and access to medicines. This suggests that these factors are key priority areas for future policy and strategy development.

1.3 Detailed analysis of factor importance by innovation type

1.3.1 Most important factors for early stage R&D

Figure 6: Most important factors for early stage R&D. N shows the total number of votes, each stakeholder was asked to vote for three factors

N = 84

The leading factor in driving early stage R&D is very clearly academic & leading edge science. Stakeholders reported unique science is a bigger factor than general sentiment towards a country when it comes to investment decisions in the ‘R’ in ‘R&D’. The three most important factors are: academic & leading edge science (29%), workforce & skills (15%), patient access to medicines and clinical trials infrastructure (joint third – 12%).

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4 Top factors only are shown in each chart. The twelve factors are: academic & leading edge science, clinical trials infrastructure, digital & data, fiscal incentives, funding & VC investment, infrastructure, international & regional collaboration, patient access to medicines, Pharmaceutical industry presence, soft factors, trade & export conditions and workforce & skills.
1.3.2 Most important factors for late stage R&D

Figure 7: Most important factors for late stage R&D. N shows the total number of votes, each stakeholder was asked to vote for three factors

N = 80

Source: PwC Strategy& interviews, Feb. 2017

5 Top factors only are shown in each chart. The twelve factors are: academic & leading edge science, clinical trials infrastructure, digital & data, fiscal incentives, funding & VC investment, infrastructure, international & regional collaboration, patient access to medicines, pharmaceutical industry presence, soft factors, trade & export conditions and workforce & skills
Late stage R&D is primarily driven by clinical trials infrastructure (23%), patient access to medicines and academic & leading edge science (joint second – 19%), with digital & data and workforce & skills joint third (11%).

“We world renowned centres of excellence and thought leaders make a very big difference in terms of our trial investments.”

Global Pharmaceutical Company

“As a company we are very interested in value based healthcare, changing the care setting and patient experience, measuring the real world outcomes associated with that. There’s huge interest in that in our company. No interest in doing that where there’s not commercial value.”

Global Biotech

This is the innovation area where access to medicines is rated highest (joint second most important factor). Stakeholders reported several reasons for this including: proximity to market, the direct impact of the comparability of the standard of care for global markets and ethical and cost issues for trial patients if access is not granted.

Stakeholders also highlighted that clinical trial activity and resulting investment is highly mobile and competitive, and there is no guarantee therefore, that the UK would be a future destination for pivotal large scale Phase III trials, where there are economic benefits to the NHS since treatment and drug costs are borne by the trial sponsor.

“We make decisions on research and investment based on access... we won’t be able to do clinical trials if the standard of care is worse than other developed countries.”

Global Pharmaceutical Company

“When you enrol patients into a trial and you finish a trial and there is never access, then that is a big problem. What do you do with these patients?”

Global Biotech

1.3.3 Most important factors\(^7\) for early stage R&D by stakeholder group\(^8\)

Figure 8: Most important factors for early stage R&D amongst academics, small biotech companies, venture capital (VC) firms and other influencers. N shows the total number of votes, each stakeholder was asked to vote for three factors

N = 35

Source: PwC Strategy\& interviews, Feb. 2017

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\(^6\) Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals

\(^7\) Top factors only are shown in each chart. The twelve factors are: academic & leading edge science, clinical trials infrastructure, digital & data, fiscal incentives, funding & VC investment, infrastructure, international & regional collaboration, patient access to medicines, pharmaceutical industry presence, soft factors, trade & export conditions and workforce & skills

\(^8\) These stakeholders were asked about R&D only
Small biotech companies, venture capital (VC) firms, academics and others prioritised funding & investment (14%) and international & regional collaboration (9%) more so than pharmaceutical companies and large biotechs in early stage R&D.

“[We] need the academic/industrial collaboration, but also need the collaboration between academics. The international and regional collaboration/bioclusters piece is very important.”

Small Biotech

1.3.4 Most important factors for late stage R&D by stakeholder group

Figure 9: Most important factors for late stage R&D amongst academics, small biotechs, VC firms and other influencers. N shows the total number of votes, each stakeholder was asked to vote for three factors

N = 33

In late stage R&D, non-pharmaceutical and large biotech stakeholders consider digital & data (18%) the joint most important factor, replacing access to medicines in the overall results. One of the reasons given for digital and data importance was that small biotech firms look to more easily work with hospitals to identify patient cohorts, with data being a key enabler to identify patients for clinical trials.

“Digital and data for trials is really important, particularly Phase II and III clinical trials, when it comes to matching new interventions and products to the right patient cohorts.”

Academic

“In terms of digital & data, products need to be more aligned to unmet need, and be able to understand how the medicines are working in the real world, [data sets] can be curated outside the public sector, e.g. by charities. But large Pharma presence is critical for capabilities development and assets.”

Influencer (biocluster)

9 Top factors only are shown in each chart. The twelve factors are: academic & leading edge science, clinical trials infrastructure, digital & data, fiscal incentives, funding & VC investment, infrastructure, international & regional collaboration, patient access to medicines, pharmaceutical industry presence, soft factors, trade & export conditions and workforce & skills
1.3.5 Most important factors\textsuperscript{10} for advanced therapy medicinal products manufacturing

Figure 10: Most important factors for advanced therapy medicinal products manufacturing. N shows the total number of votes, each stakeholder was asked to vote for three factors. N = 44

<table>
<thead>
<tr>
<th>Factor</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Workforce &amp; skills</td>
<td>36%</td>
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<tr>
<td>Fiscal incentives</td>
<td>30%</td>
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<tr>
<td>Infrastructure</td>
<td>11%</td>
</tr>
<tr>
<td>Access to medicines</td>
<td>9%</td>
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<tr>
<td>Other factors</td>
<td>14%</td>
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</table>

For advanced therapy medicinal products manufacturing (which includes breakthrough cell and gene therapies), the most important factors were workforce & skills (36%), fiscal incentives (30%) and infrastructure (11%). Across manufacturing of advanced therapy medicinal products and other highly specialised products (such as biologics), there are factors of common importance e.g. fiscal incentives such as taxation, and workforce & skills. However, the manufacturing of advanced therapy medicinal products involves the most highly specialised skills which are not found in a single country, requiring the ability to attract top global talent.

Access was referenced as an important factor for advanced therapy medicinal products manufacturing. In areas where the patient's own cells are used, co-location of manufacturing, R&D and specialist treatment facilities is an advantage.

“A big factor is availability of skills, especially for manufacturing which is highly specialised.”

Global Pharmaceutical Company

“We have just built new plants and fiscal incentives have been very important in that. Also workforce and skills come in on that too. Typically [we are] no longer looking for a large number of unskilled workers, [but] looking for a smaller, highly trained workforce.”

Global Pharmaceutical Company

“We incentives for manufacturing... have to be access and uptake. Just focusing on corporation tax is good, but that's not the end stage. If you can link criteria or incentives around [what] you discover/manufacture here, there's an additional value here for UK PLC.”

Global Pharmaceutical Company

\textsuperscript{10} Top factors only are shown in each chart. The twelve factors are: academic & leading edge science, clinical trials infrastructure, digital & data, fiscal incentives, funding & VC investment, infrastructure, international & regional collaboration, patient access to medicines, pharmaceutical industry presence, soft factors, trade & export conditions and workforce & skills.
1.3.6 Most important factors\textsuperscript{11} for specialist ‘above-country’ commercial activities\textsuperscript{12}

For commercial activities, \textit{workforce & skills} (30\% of votes), \textit{fiscal incentives} (18\%), \textit{infrastructure} (15\%) and \textit{access to medicines} (9\%) are the most important factors. Specialist commercial teams travel between global headquarters and other offices, which relies on good infrastructure e.g. air and rail hubs.

\textbf{Case study Gene therapy}\textsuperscript{12}: Gene therapy is the delivery of nucleic acids to replace, correct or inactivate the genes causing a disease. Gene delivery is usually via a viral vector – a non-pathogenic viral strain. Some gene therapies require the patient’s own cells to be modified outside the body, which often requires patients to be near production. One example is Strimvelis, which received EMA approval in 2016 for the treatment of ADA-SCID. Development originally began in Milan by Ospedale San Raffaele (a research hospital) and Fondazione Telethon (a biomedical charity), but in 2010 they formed a collaboration with GSK and the biotech company MolMed S.p.A. Their joint expertise, and an access environment that allows for co-location of patient treatment centres and gene therapy production, now makes Milan, Italy a hub for gene therapy research and advanced patient treatment.

\textbf{Figure 11: Most important factors to innovation in specialist ‘above-country’ commercial activities.} N shows the total number of votes, each stakeholder was asked to vote for three factors

\begin{figure}[ht]
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Most important factors to innovation in specialist ‘above-country’ commercial activities. N shows the total number of votes, each stakeholder was asked to vote for three factors}
\end{figure}

\begin{itemize}
\item Workforce & skills
\item Fiscal incentives
\item Infrastructure
\item Access to medicines
\item Other factors
\end{itemize}

\textbf{Source: PwC Strategy\& interviews, Feb. 2017}

\textsuperscript{11} Top factors only are shown in each chart. The twelve factors are: academic & leading edge science, clinical trials infrastructure, digital & data, fiscal incentives, funding & VC investment, infrastructure, international & regional collaboration, patient access to medicines, pharmaceutical industry presence, soft factors, trade & export conditions and workforce & skills

\textsuperscript{12} ‘Above-country’ commercial functions are those with regional or global reach, such as regulatory or analytical expertise

\textsuperscript{13} Sources: GSK website, EMA guidelines on gene therapy medicinal products (2015), PwC Strategy\& analysis. Data on file
Access was referenced as particularly important due to global sentiment and the relative priority of each market to the global senior team. Also in practical terms, some regulatory functions are located more closely to regulatory bodies. In Europe, this is the European Medicines Agency (EMA), which currently resides in London, but there is uncertainty about the future location following the Brexit Referendum result.

“We are considering relocating commercial functions... criteria are workforce and skills i.e. talent availability. We are trying to build a very strong talent base.”  
**Global Pharmaceutical Company**

“We look for income tax, an overall economy that works. No industry relation issues, no strikes, and good transport. [Work] permit for someone abroad [are obtained] very easily.”
**Global Pharmaceutical Company**

“In terms of an international competitiveness perspective... a 3rd runway at Heathrow is really important, [it] is absolutely pivotal [and] investment into rail infrastructure continues to be important.”
**Influencer (biocluster)**

“Access is particularly important [to above country commercial activities] as it creates a lot of sentiment, and people do make decisions based on positive and negative sentiment... there is a lot of disappointment in the UK.”
**Global Biotech**

1.4 Conclusion

To have a globally competitive life sciences ecosystem, critical factors are workforce & skills, academic & leading edge science, and access to medicines.

In the next section this report explores UK current competitiveness on these factors, with a focus on where to lead and close gaps.
Chapter 2 – How is the UK performing compared with other global life science hubs?
The UK is a leader in science and skills. It could capitalise on the NHS and The City’s financial standing to improve its global standing in digital & data, clinical trials infrastructure and funding & investment. The UK trails other markets significantly in patient access to medicines, and improving performance would enhance UK capabilities and R&D.

2.1 Methodology

The UK was benchmarked on twelve ecosystem factors (outlined in Chapter 1) against six countries: France (FR), Germany (DE), Japan (JP), Singapore (SG), Switzerland (CH) and the US. These countries were chosen based on their reputations as leading life sciences markets, for a range of reasons e.g. the US is the largest pharmaceutical market by value, Switzerland is well known for its tax incentives and large pharmaceutical companies presence, whereas Singapore is a popular destination for clinical trials and acts as a gateway to Asia for life sciences companies. These countries broadly align with the selected countries for benchmarking by the Office for Life Sciences (OLS) Industrial Strategy.

Of the twelve ecosystem factors, ten had sufficient data to be quantifiable and comparable. The exceptions were soft factors and trade and export conditions. Each quantifiable ecosystem factor was assigned quantitative benchmarks based on the literature review and the data available. These benchmarks were indexed on a scale of 0 – 100, with 100 being the best performing data point, and then averaged over each factor to give an overall indication of comparative performance across the life sciences innovation ecosystem.

The data for individual benchmarks were sourced from a range of internal and published sources, and can be found in Appendix C. Where data have been collected for the Industrial Strategy Stakeholder Group, these have been leveraged as the most up to date figure for relevant countries, and sourced as “UK Life Sciences Industrial Strategy: Initial Findings”.

14 The benchmarked countries selected for this report are a subset of the countries included in the Office for Life Sciences Industrial Strategy (in progress at the time of writing), with the addition of Japan.
2.2 UK performance: overview

The UK shows a clear strength in its science base, outperforming the majority of peers in many of the academic & leading edge science and workforce & skills benchmarks. Additional strengths include the size and reputation of life sciences clusters built around world-renowned institutions. Despite these assets, the innovation ecosystem must be considered holistically, and there are also areas where the UK falls behind. UK levels of industry funding and venture capital (VC) are relatively competitive, but public sector funding of life sciences trails peers. Infrastructure (e.g. air and rail) is a key driver of innovation when it comes to ease of travel for employees, and although the UK is objectively good, it is outperformed by all other benchmarked countries.

Patient access to medicines is the one factor where the UK lags substantially. On average, patients in Switzerland have access to seven times the medicines available to UK patients, based on volume per capita. The detailed findings from the data analysis on patient access can be found in Chapter 3.

Figure 12: Performance of benchmarked countries across the ten quantifiable factors

Sources: PwC Strategy& analysis, various, depending on individual benchmarks, detailed in Appendix C

15 Countries are not shown on the summary if good quality data was not available for a particular factor
2.3 Detailed analysis of UK performance by category

2.3.1 Science, innovation and scale

Figure 13: Life sciences publications and new PhDs in science, maths and computing by country per million pop.

The UK is a world-leading destination for academic & leading edge science with high productivity in life sciences publications, top global life sciences universities and high numbers of PhDs. This reputation, backed up by the data, positions the UK highly as a prime destination to attract the top talent, and investment in early stage R&D. The UK is broadly in line with the US and France in the number of researchers in R&D.

Figure 15: Researchers in R&D per million pop.

Sources: World Bank Development Indicators, PwC Strategy & analysis

Figure 16: Biotech firms per million pop.\(^{16}\)

Sources: OECD Key Biotechnology Indicators, PwC Strategy & analysis

\(^{16}\) Data on biotech firms was not available for Singapore
The change in position compared to performance on publications and PhDs suggests top talent is drawn to other markets despite the UK’s “head start” on academic science. This echoes the views of stakeholders interviewed, who remarked UK translation of science does not reflect the strength of its science base. Singapore leads on researchers in R&D, reflecting stakeholder opinions that Singapore has a very strong and highly skilled life sciences workforce.

Looking at the number of Biotech firms per million population, the UK is broadly in line with Germany, but trails France, Switzerland and the US. This could be another indicator of the UK trailing peers in translation of science. Europe struggles to compete against the enormity of the US market, with its 36 biotech firms per million pop. and leading cluster regions on the East and West Coasts. The Massachusetts biocluster alone is home to almost 1000 establishments, triple the size of the UK’s Cambridge biocluster17. The network effects created by the US market make it difficult to compete on talent acquisition.

In summary, the UK has world leading capabilities in academic & leading edge science and workforce & skills. Maintaining and if possible expanding this leadership is critical to innovation in early stage R&D. By seeking to enhance excellence through international & regional collaborations, applying best practice from the East Coast and West Coast US bioclusters, the UK can enhance global competitiveness.

2.3.2 Economic and political environment

Singapore, Switzerland and the US are ahead of all other benchmarked countries in terms of their economic and political environments, with high levels of funding and investment, attractive fiscal incentives, and well developed infrastructure.

Figure 17: Industry and public spend on life sciences R&D18

![Chart showing industry and public spend on life sciences R&D](chart.png)

Sources: UK Life Sciences Industrial Strategy: Initial Findings, PwC Strategy& analysis

Figure 18: Investment from venture financing19

![Chart showing investment from venture financing](chart.png)

Sources: EvaluatePharma, PwC Strategy& analysis

From the figure above, it is clear that Switzerland leads in industry investment in life sciences R&D, while Singapore dominates in public sector funding. Switzerland is well known for its pharmaceutical industry due to the presence of a number of large pharmaceutical companies, whereas the Economic

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18 Data in industry and public spend was not available for Japan
19 Data on the level of venture financing was not available for Singapore
Development Board (EDB) in Singapore spends c.$1.05bn USD annually on biomedical R&D\textsuperscript{20}, making it an attractive country for pharmaceutical investments. Companies mentioned the impressive speed, professionalism and skills in Singaporean Government and EDB, which influenced investment decisions. The US is also a significant public funder of R&D, with the NIH investing c.$32.3bn USD in medical research per year\textsuperscript{21}, which is not obvious from the figure as the data are skewed by population effects. The UK in comparison trails all other countries in public sector spend, but is slightly above France and Germany on industry spend.

The data show Switzerland performing well in venture financing investment, although this was not further evidenced in interviews. The UK has higher venture financing investment levels compared to France and Germany. Stakeholders recognised this but felt the funding process in the UK is disjointed, which means that research can get to a certain stage only to find there is no money to get it to the next point. This issue was reflected by stakeholders.

"The gap in funding series C/D is absolutely enormous… [organisations] have to exit, [and drugs] which may have originated in the UK often ends up in the hands of US Pharmaceutical companies."

Small Biotech

In terms of corporate tax rates and life sciences specific fiscal incentives, the UK remains competitive, but is again overshadowed by Singapore and Switzerland. For example, the statutory corporate tax rate in the UK will be 19% from 1 April 2017, reducing to 17% by 2020, but in Singapore it is already 17%, and can be as low as 11.5% in Switzerland depending on the canton and subject to anticipated Swiss tax reform\textsuperscript{22}. Note that while the US is not currently as competitive in its fiscal incentives, with the recent changes in US administration following the presidential elections, the fiscal environment may change, especially to incentivise repatriation of US manufacturing.

In summary, the UK can build excellence in funding & investment. For example by addressing the levels of public funding which are currently trailing all other markets (particularly Singapore and the US, noting that high funding levels are skewed by population effects) and encouraging further patient capital and venture capital (VC) funding. Leveraging the strength of The City and VC market to develop a seamless end-to end solution for biotech firms is also an opportunity unique to the UK.

2.3.3 Health and commercial

Figure 19: Index median cost per visit for clinical trials, benchmarked against the UK = 100\textsuperscript{23} (2013-15)

\begin{figure}
\centering
\includegraphics[width=\textwidth]{index_median_cost_per_visit}
\caption{Index median cost per visit for clinical trials, benchmarked against the UK = 100\textsuperscript{23} (2013-15)}
\end{figure}

Sources: Parexel Biopharmaceutical R&D Statistical Sourcebook 2016/17, PwC Strategy\& analysis

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\textsuperscript{20} Converted from $1.49bn Singaporean dollars using the exchange rate 1 SGD : 0.71 USD. Source: EDB website

\textsuperscript{21} Source: NIH website

\textsuperscript{22} Source: PwC World Wide Tax Summaries, PwC Tax experts’ analysis. Data on file

\textsuperscript{23} Data on index median cost per visit was unavailable for Japan or Switzerland
Figure 20: Clinical trials per million pop. by phase and country

Sources: Clinicaltrials.gov, PwC Strategy& analysis

Life sciences R&D includes early stage discovery science in laboratories, pre-clinical testing and clinical trial activity (Phase I – III). Late stage clinical trials provide substantial inward investments and benefits to the both patients and the health system.

France is an attractive location for late stage clinical trials, which may be driven by its low average cost. The UK has higher costs relative to France and Germany. Stakeholders gave three potential explanations for this: first the low availability of Standard of Care therapies on the NHS which requires pharmaceutical companies to fund an additional therapy, second set up times to progress through ethics committees and third, higher costs of Principle Investigators.

Switzerland is the most active market for Phase II and III clinical trial activity, mirroring anecdotal evidence obtained in interviews. Singapore is also highly competitive, which may be due to its diverse population representing the wide range of ethnic groups found across Asia and its good clinical practice, making it an attractive location for bridging trials into the Asia-Pacific region. Both countries’ results are likely to be slightly skewed due to population effects.

The UK is fourth highest for Phase I trials, and fifth highest for Phases II and III. The higher levels of Phase I and Phase II trials reflect strengths in science, however lower performance in Phase III, stakeholders reported is linked to the access environment.

The issue of access to Standard of Care in the UK was regularly raised throughout the interviews. Stakeholders reported that the UK Standard of Care was often lower than the global standard. They acknowledged the lack of comparable Standard of Care could be managed for NICE’s HTA assessment (through the use of modelling, although this creates added uncertainty which may impact outcomes). However it was stressed that UK clinical trials are part of a global programme used for US, Japanese and many other regulators, not primarily for UK reimbursement. Stakeholders found that in other markets the Standard of Care is necessary for either Market Authorisation or reimbursement. Furthermore, stakeholders commented that although Standard of Care usually refers to the therapy, problems also arise where the UK care pathway does not meet global standards.

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24 Drug discovery – tests of molecular compounds to find possible beneficial effects against diseases, Pre-clinical – In vivo & in vitro testing (in vitro refers to testing in a test tube, in vivo means testing in a living organism), Phase I – tests in volunteers to determine safety and dosing, Phase II – tests in patients to determine efficacy, Phase III – tests in patients on efficacy vs. standard of care. Sources: www.fda.gov, PwC Strategy

25 Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals.
In addition to the practical issues faced by the Standard of Care being unavailable, stakeholders also mentioned the ethical issues surrounding conducting clinical trials in countries where access is challenging. Providing patients with a treatment during trials that others are unlikely to access on the NHS afterwards poses ethical challenges, especially for chronic diseases, leaving companies with a difficult decision to accept this challenge or to site trials in other locations.

“If you know you will have difficulty after a trial because you don’t think you will get access for a few years, it’s unethical.”

Global Pharmaceutical Company

Stakeholders also said that trials are often cited in the UK to access world-leading key opinion leaders (KOLs). This familiarises them with novel treatments and their results, which can then be spread globally at international conferences. However some stakeholders mentioned that the reputation of UK KOLs is beginning to diminish, as they do not have enough access or experience with the global Standards of Care.

Furthermore, the UK has unmet potential to be globally competitive in Real World Evidence (RWE), as one of the few countries with a single healthcare system. Stakeholders expressed the opinion that infrastructure in the NHS is not yet sufficient to realise its full capacity in RWE.

Case study Standard of Care:
Stakeholders have cited that the Standard of Care in the UK is a particular problem in oncology. For example, NICE has not approved Avastin (bevacizumab), or Abraxane (paclitaxel) for colorectal cancer, and pancreatic cancer, respectively. Pharmaceutical companies gave these products as examples of where the lack of UK access has resulted in clinical trials being sited elsewhere. In the particular case of Avastin (bevacizumab), which was first approved by the EMA and US FDA in 2005 and 2004 respectively, UK patients do not have access to Avastin (bevacizumab) for any indication on the NHS.

In addition to the practical issues faced by the Standard of Care being unavailable, stakeholders also mentioned the ethical issues surrounding... If the Standard of Care or head-to-head comparator in the US/Japan isn’t part of the standard patient pathway in the UK, that’s when the UK becomes less and less attractive.”

Global Pharmaceutical Company

“It’s not just the Standard of Care, [it’s] also the infrastructure to deal with these technologies. During the induction phase [for trialling a particular product] you need 7 days a week therapy, that wasn’t possible in the UK.”

Global Pharmaceutical Company

“Increasingly [it’s] not just medicine and the Standard of Care, [it] could be the diagnostic panel, radiotherapy protocol, or in a precision medicine, [whether] they can get the right patient groups quickly.”

Global Pharmaceutical Company

“In the] UK, how do we handle these end of trial situations? [It’s an] ethical issue. Do we really want to get ourselves in a position where we have to supply drugs beyond the end of a trial for chronic diseases?”

Global Biotech

Stakeholders also said that trials are often cited in the UK to access world-leading key opinion leaders (KOLs). This familiarises them with novel treatments and their results, which can then be spread globally at international conferences. However some stakeholders mentioned that the reputation of UK KOLs is beginning to diminish, as they do not have enough access or experience with the global Standards of Care.

Furthermore, the UK has unmet potential to be globally competitive in Real World Evidence (RWE), as one of the few countries with a single healthcare system. Stakeholders expressed the opinion that infrastructure in the NHS is not yet sufficient to realise its full capacity in RWE.

26 Sources: PwC Strategy& interviews, Feb. 2017, EMA, FDA, NICE. Data on file
Despite this general trend, there are certain examples of the UK embracing and leveraging RWE, such as the Clinical Practice Datalink (CPRD), Hospital episode Statistics (HES), and the Connected Health Cities initiative in the North of England. However, other countries such as Sweden, Italy and the US were cited as being further ahead in this area.

In summary, the UK has potential to be in a ‘best-in-class’ position on clinical trials infrastructure and digital & data. Currently UK performance sits within a cluster of other markets like France and Germany. If able to leverage the unique structure of the NHS, the UK could be world leading.

There is one critical factor where the UK is significantly trailing the performance of other markets: patient access to medicines. Stakeholders repeatedly raised concerns that the UK trails others countries on access and uptake and that this impacts global investment decisions. This analysis found that this factor had a detrimental effect on all investments including R&D, manufacturing and commercial. This suggests current poor performance in this area impacts the inflows of investment into other core ecosystem areas such as science, skills, clinical trials infrastructure etc.

Case study Real World Evidence (RWE): RWE refers to data and insights that is not captured as part of a clinical trial setting. It can include data from patient disease registries, electronic health records, insurance claims data and patient reported outcomes (PROMS). The purpose of RWE is often to improve healthcare practice and to demonstrate outcomes linked to drug reimbursement. Currently a number of other countries are developing data sets and disease registries to better support clinical research and monitor health outcomes. For example in Sweden, there are 104 national quality registers to monitor care and treatment. The Rheumatology Quality Register (1995-) contains data on the symptoms and treatment outcomes of 66,000 patients (about 85% of people in Sweden with rheumatoid arthritis). Data is fed into a “dashboard” and used to support care. PROMs are tracked over time. In Italy the Italian Medicines Agency AIFA (equivalent of NICE) has managed patient registries since 2005 which are used to support conditional reimbursement and monitor performance. In the US, NCI-MATCH claims to be the largest, most rigorous precision oncology trial ever. It uses RWE to screen 3000 patients with genetic mutations across 2400 US sites to provide them with access to the latest therapies and to monitor outcomes in the real world. The UK is not yet demonstrating the same level of capability, although GSK led a pioneering RWE study of 2800 patients with Chronic Obstructive Pulmonary Disease (COPD) patients in Salford to demonstrate the effectiveness of a new product in a real world setting.

2.4 Conclusion

The UK has strengths and weaknesses contributing to its life sciences ecosystem. All factors in this holistic ecosystem play individual but important and interconnected roles to maintain a globally competitive sector for investment.

“Generally the UK has built a really bad reputation on adoption of innovation, which creates a very negative sentiment when it comes to investment decisions regarding R&D.”

Global Pharmaceutical Company

“[We’re] at a tipping point… where the sentiment on access and approach to innovation is really influencing investment.”

Global Pharmaceutical Company
Chapter 3 – What is the UK access gap?
UK patients have up to 75% lower uptake of new medicines (by volume per capita) in their first year of launch and it takes on average almost two years to catch up with the next lowest uptake country. Even with NICE approval and ‘novel’ designation UK patients have up to 64% lower uptake (by volume per capita). The gap is also seen across multiple disease areas.

### 3.1 Methodology

In order to compare quantitatively patient access to medicines across benchmarked countries, sales volumes of medicines per capita were used as a proxy measure. Raw sales data was accessed via QuintilesIMS.

The analysis in this chapter is based on quarterly sales volumes in standard units. The analysis included all patented products launched over the last five years (2011 – 2016), with at least £100,000 in revenue per annum (to filter out products with limited patient uptake globally). This provided a provisional list of 339 products. From this provisional list, products were filtered to include those with sufficient comparable data for the first year post-launch, i.e. data was available for at least four quarters, for at least four of the six benchmarked countries, which resulted in 88 products. Of those 88 products, products were further removed if they were medical devices or no longer had Market Authorisation from the European Medicines Agency (EMA), producing a general basket of 76 products. The details of all 76 products can be found in Appendix D.

Further analysis of the data included analysis by US ‘novel’ product definition, UK NICE appraisal status (NICE recommended or NICE not recommended only) and analysis by disease area.

- The term ‘Novel’ products is a US definition and includes products defined with the US FDA’s CDER Novel Drug designation, including Fast Track, Breakthrough, Accelerated Approval and Priority Review.

- NICE appraisal status divides the basket into six categories: recommended, recommended for use within the Cancer Drug Fund (CDF), optimised, only in research, not recommended, and not assessed (which includes products currently pending assessment, and those that do not need NICE assessment). No products in the analysis were classified as ‘only in research’, therefore this category is disregarded in the analysis. Furthermore, NICE considers both ‘recommended’ and ‘optimised’ products to be recommended, however where this analysis refers to ‘recommended’ products, it refers to those with a full NICE recommendation only.

- Indications are mapped to one of the following disease areas: cardiovascular and metabolic, immunology & inflammation and ocular diseases, infectious diseases, neurology, oncology, respiratory, and miscellaneous.

Where there are fewer than the total six benchmarked countries shown in figures, this is due to insufficient data. Unless stated otherwise, all comparisons are over the first year post-launch. All launch years have been normalised, i.e. regardless of the year of launch, the first four quarters post-launch are taken to be the “first year”.

For more details on the methodology, the key assumptions made and the definition of standard units, please refer to Appendix E.

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28 Benchmark countries are: France, Germany, Japan, Singapore, Switzerland, UK and US
29 Standard Units are the smallest common dose of a product formulation and are more appropriate when comparing sales of products with different formulations
30 Singapore was removed from the access benchmark as data was only provided for c.40 products, making it unfeasible to compare across other countries

31 The US FDA novel drugs definition is as follows: ‘Novel drugs are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient care and public health. New molecular entities (NMEs) have chemical structures that have never been approved before. However, in some cases an NME may have actions similar to earlier drugs and may not necessarily offer unique clinical advantages over existing therapies.’ Source: [www.fda.gov](http://www.fda.gov) [accessed 10 Feb. 2017]

32 Optimised means NICE has recommended the medicine for a smaller subset of patients than originally stated by the marketing authorisation, e.g. a medicine is only cost-effective as a treatment option for a specific group of people, for example, those who are resistant to or can’t tolerate other drugs. Source: [www.nice.org.uk](http://www.nice.org.uk) [accessed 01 April 2017]
3.2 UK performance on access

3.2.1 Uptake of patented products launched 2011 – 2016

Figure 21: Uptake of 76 patented drugs launched 2011 – 2016 by volume pmp\(^{33}\), first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis

Analysis of access across the entire basket of 76 products shows consistently poor access in the UK compared to benchmarked countries.

The scale of the differential between the UK and the average across all benchmarked countries is c.75% (by volume per capita). Switzerland has the highest access in terms of volume per capita, seven times that of the UK. France and Germany are comparable to the UK in terms of population and GDP per capita, but Germany has almost five times greater access and France has over three times greater access. The closest to the UK is Japan, with over twice the access (though Japan has fewer products launched in the market).

3.2.2 Uptake of novel drugs

Figure 22: Uptake of 45 novel\(^{34}\) drugs launched 2011 – 2016 by volume per capita, first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis

“Novel product” is a US definition. These products are categorised by the FDA Center for Drug Evaluation and Research (CDER). Although this definition is not applicable in the UK, it provides a useful way of identifying therapies which are “among the more innovative products that often help advance clinical care to another level”\(^{35}\). By comparing access across novel drugs only, we see the UK also trails other countries.

To understand what is driving poor UK uptake of these novel medicines, a further split of products was performed. These 45 novel products can be split by their NICE appraisal status:

- 20 are NICE recommended
- 10 are optimised, i.e. recommended for a smaller subset of patients than originally stated by the marketing authorisation
- 15 are ‘other’ (5 not recommended, 6 pending assessment, 4 did not require NICE approval)

Comparing NICE recommended and not recommended products separately shows an interesting picture:

\(^{33}\) pmp: per million population

\(^{34}\) Janet Woodcock, M.D., Director, Centre for Drug Evaluation and Research, 2016 Novel Drugs Summary. Source: www.fda.gov

\(^{35}\) Janet Woodcock, M.D., Director, Centre for Drug Evaluation and Research, 2016 Novel Drugs Summary. Source: www.fda.gov
Figure 23: Uptake of 20 NICE recommended novel drugs launched 2011 – 2016 by volume pmp, first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis

Unsurprisingly the uptake of products not recommended by NICE is extremely low compared to peers. However, looking at Figure 23, it is clear that despite full recommendations from NICE, UK access still remains poor at up to 64% less than the average across all benchmarked countries.

This suggests that although NICE appraisal is an additional barrier to access, UK access is further slowed by NHS commissioning and/or prescribing decisions, which reflects the opinions gathered from stakeholder interviews.

3.2.3 The most challenging areas of access

Note that although this report is not a detailed review of the UK access system and processes, stakeholders offered a range of opinions as to why there is an access gap. Whilst sharing these views, this report recognises the challenges faced by the NHS and the efforts underway to address the points raised below.

Some stakeholders recognised the positive aspects of the NICE assessment process, for example that it is transparent, robust and independent, and sets a clear 90 day mandate for the NHS to make available recommended technologies. However, of the 33 stakeholders, 27% stated the primary challenge to access lies with NICE. Stakeholders commented that the focus on the cost/QALY metric, is not suitable for all specialised therapies (e.g. for targeted groups or multiple indications).

Stakeholders voiced concerns that NHS England (NHSE) often does not uphold the NICE 90 day mandate on availability, leading to unpredictability for both patients and manufacturers. At the time of publication a budget impact test was announced. The test will enable NHSE to opt out of the 90 day mandate and introduce medicines costing over £20m (in one of the first three years of launch) in a phased way over three years. 15% of stakeholders cited that access and uptake of new medicines by the NHS as the greatest challenge in the UK access environment. Reasons given

36 Note: NICE analysis does not use the same definition of ‘recommended’ that is used in this analysis. NICE considers ‘optimised’ products to be recommended, however this analysis considers the two as separate categories. Figure 23 only shows data for products with a full NICE recommendation, and excludes NICE ‘optimised’ products

37 Note: NICE analysis does not use the same definition of ‘not recommended’ that is used in this analysis. NICE considers products recommended for use within the Cancer Drug Fund (CDF) to be recommended, however this not recommended analysis includes 1 product, Kadcyla (trastuzumab emtansine), made available to UK patients through the Cancer Drugs Fund

included: opaque processes, duplication across Clinical Commissioning Groups (CCGs) and resistance to outcomes-based pricing models. If adopted, outcomes based pricing could provide value for money and minimise risk and budget impact over time.

A small number of stakeholders raised concerns that clinicians often prioritised NHS budget containment over patient access to newer treatments.

The most pressing challenge stated by the majority of stakeholders (52%) was the need to improve coordination across the overall process. By improving communication between NICE, NHSE, CCGs and providers, uncertainty could be reduced and additional delays in access could be avoided (as providers negotiate at each level). In particular, pharmaceutical companies expressed frustration in engaging separately, with over 200 CCGs across the country.

Shown below are some selected quotes from stakeholders concerning areas of the UK access environment that they think are contributing to the access gap.

Figure 25: Quotes from stakeholder interviews, in response to the question: “Which part of access is most challenging in the UK?”

“NICE has some positives – it is a fair, national approach across the market [and] once a decision is made, within 90 days [that] gives equal access across the country.”

Global Pharmaceutical Company

“Undoubtedly the most critical is a combination of the NICE decision and the reality of uptake in the NHS.”

Influencer

“All the NHS wants are simple discounts.”

Global Biotech

“If it’s a medicine paid for by CCGs, you can’t engage with over 200 CCGs all across the UK!”

Global Biotech

“It’s getting worse where NHS is managing the process, specialist commissioning is almost a lottery. NICE is tough, but transparent.”

Global Biotech

“Doctors in the UK feel very much like guardians of the NHS… Even where there is a choice on what to use that is best for patients, UK clinicians will still try to save money.”

Global Pharmaceutical Company

In order to address these challenges and improve patient access to medicines, stakeholders suggested increasing collaboration and connectivity between different parts of the UK health system, as well as increased acceptance of outcomes-based pricing models. This will be explored further in Chapter 5.

3.2.4 Uptake by therapeutic area

Splitting the products by the diseases they target (i.e. therapeutic area) demonstrates that the UK’s access issue is a prominent challenge across all diseases. The differentials between the UK and the average across benchmarked countries in the first year post-launch ranges from up to 49% for oncology, to, up to 89% in hepatitis C.

Figure 26: Uptake of 31 oncology drugs launched 2011 – 2016 by volume pmp, first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis

The proportion of oncology products used is broadly in line with other countries, but at considerably lower levels. The US is surprisingly low on this metric, despite performing well on the uptake of novel oncology products. This could be due to population effects.
**Case study Oncology**

**Zytiga (abiraterone acetate):** This is the most commonly used oncology product across four of the benchmarked countries. It received marketing authorisation from both the US FDA and the EMA in 2011 for the treatment of metastatic castration resistant prostate cancer (mCRPC). It was originally not recommended by NICE for use by the NHS as it was not deemed cost-effective. However following a discount on the list price from the manufacturer, NICE approved it in 2012, as a second-line treatment after chemotherapy. After a further change to the commercial arrangements in July 2016, NICE recommended its use as a first-line treatment, however, only when the company provides Zytiga (abiraterone acetate) in accordance with the commercial access arrangement as agreed with NHS England. This is over three years after it became routinely available in benchmarked countries such as France and Germany.

**Case study Hepatitis C**

**Sovaldi (sofosbuvir) and Harvoni (ledipasvir/sofosbuvir):** Hepatitis C products can offer a cure to patients in twelve weeks. In their respective first years post-launch, uptake of Sovaldi (sofosbuvir) and Harvoni (ledipasvir/sofosbuvir) was more than six times lower in the UK compared to France, and more than seven times lower compared to Germany. Both of these products are optimised by NICE, recommending use by genotype and severity. There were delays to NHSE commissioning guidance for hepatitis C treatments. Although these products have particularly high price points, this was a common challenge across countries.

As stated previously, UK patients have far lower access to hepatitis C drugs.

---

**Figure 27:** Uptake of 6 hepatitis C drugs launched 2011 – 2016 by volume pmp, first year post-launch

<table>
<thead>
<tr>
<th>Country</th>
<th># standard units purchased (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>119</td>
</tr>
<tr>
<td>JP</td>
<td>115</td>
</tr>
<tr>
<td>DE</td>
<td>73</td>
</tr>
<tr>
<td>CH</td>
<td>54</td>
</tr>
<tr>
<td>FR</td>
<td>47</td>
</tr>
<tr>
<td>UK</td>
<td>7</td>
</tr>
</tbody>
</table>

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis, data may be skewed by low numbers of products by indication

**Figure 28:** Uptake of 7 cardiovascular drugs launched 2011 – 2016 by volume pmp, first year post-launch

<table>
<thead>
<tr>
<th>Country</th>
<th># standard units purchased (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DE</td>
<td>130</td>
</tr>
<tr>
<td>US</td>
<td>121</td>
</tr>
<tr>
<td>CH</td>
<td>71</td>
</tr>
<tr>
<td>JP</td>
<td>44</td>
</tr>
<tr>
<td>FR</td>
<td>15</td>
</tr>
<tr>
<td>UK</td>
<td>11</td>
</tr>
</tbody>
</table>

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis, data may be skewed by low numbers of products by indication

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39 Sources: NICE, www.nice.org.uk
40 Sources: QuintilesIMS, PwC Strategy & analysis. Data on file
41 Definition of Cure: Sustained Virological Response (SVR) is used to determine the Hepatitis C Virus (HCV) cure rate which is defined as HCV RNA less than LLOQ at 12 weeks after the cessation of treatment. RNA is the quantitative HCV RNA test used to measure the amount of hepatitis C virus in the blood or viral load; LLOQ is the lowest amount of HCV RNA that is in the linear range. [http://www.medicines.org.uk/emc/medicine/29471](http://www.medicines.org.uk/emc/medicine/29471). Accessed March 2017
Figure 29: Uptake of 7 metabolic drugs launched 2011 – 2016 by volume pmp, first year post-launch

Figure 30: Uptake of 6 neurology drugs launched 2011 – 2016 by volume pmp, first year post-launch

Figure 31: Uptake of 3 respiratory drugs launched 2011 – 2016 by volume pmp, first year post-launch

Figure 32: Uptake of 7 immunology & inflammation and ocular drugs launched 2011 – 2016 by volume pmp, first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis, data may be skewed by low numbers of products by indication
Figure 33: Uptake of 4 HIV drugs launched 2011 – 2016 by volume pmp, first year post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis, data may be skewed by low numbers of products by indication

Note that in some disease areas, there are a much smaller numbers of products within the analyses, which can cause a disparity in results. However, the UK’s consistently low position illustrates that access is poor across multiple diseases.

3.2.5 Uptake over time

Figure 34: Uptake of 32 patented medicines launched 2011 – 2016 by volume pmp, first three years post-launch

Sources: QuintilesIMS, MIDAS as of Q3 2016, PwC Strategy& analysis

Finally, looking at the products with comparable data over the first three years post-launch, data shows that UK access remains low and slow.

Across all patented medicines the UK uptake curve is generally shallower than comparator countries. Population adjusted volume sales in the UK reaches German levels two years post-launch. As the analysis adjusts for launch year, the period taken for NICE assessment (which can delay access by 12 months\(^{43}\)) is not taken into account, so it could be reasonably expected that other countries are using newer therapies at this point.

In the particular case of Germany, the German system often automatically reimburses products for the first year post-EMA approval before conducting any HTA assessments. This is reflected in Figure 34 where the uptake over the first four quarters post-launch is steeper.

This chart also mirrors anecdotal evidence from stakeholders that UK access can be the lowest in the EU at launch, and then by the middle of the patent period may “leapfrog” others and maintain a low-middle position.

3.3 Conclusion

The data show that regardless of product indication, NICE status, or US novel drug status, the UK is trailing benchmarked countries significantly in patient access to medicines. As one of the critical top three factors contributing to the holistic life sciences innovation ecosystem, it is important to improve the access environment. Bridging the access gap brings opportunities to benefit patients, the NHS, and the wider economy.

42 Comparable means there is data available for at least four of the benchmarked countries for the entire period of time considered, in this case three years or twelve quarters
Chapter 4 – What are the economic benefits of reducing the access gap?
If the UK improves the volume of new medicines available to patients it could better support a thriving life sciences ecosystem, stimulate healthcare improvements for patients, NHS transformation and UK R&D. Through additional R&D alone, 4000 new jobs could be created by 2021 and £705m in Gross Value Added (GVA) realised each year.

This report has demonstrated that the UK performs strongly on many of the characteristics that underpin a thriving Life Sciences sector, but that it lags significantly behind benchmarked countries in terms of access to new medicines.

Improving the UK’s access environment could support a more competitive life sciences sector, encouraging more companies to invest in the UK and expand their domestic footprint. This would in-turn boost UK employment, economic output and tax receipts.

4.1 Methodology

The interview responses from key stakeholders indicate that improved patient access to medicines would incentivise pharmaceutical companies to boost their R&D investment in the UK. Of the 33 stakeholders, 18 were pharmaceutical or global biotech representatives. Of these 13 stakeholders were able to provide quantitative inputs on their scale of this behavioural response based on two scenarios:

- **An increased access scenario** was described as: Spending on bio-pharmaceutical products and market share for newer medicines is increased, an expanded model of accelerated access is applied (similar to US FDA Breakthrough Therapy), NICE approval is accelerated to earlier R&D stage (Ph. II), reimbursement is linked to Real World Evidence (RWE) and the UK becomes a leader in innovative pricing and rewards innovation.

- **A decreased access scenario** in which the UK ecosystem worsens through: Spending on bio-pharmaceutical products staying flat or contracting, budgets failing to reflect aging population pressures, one or two leading medicines fail to obtain reimbursement or require sizeable price reductions in contrast to other major markets, managed access to cancer drugs funding with no revenue forecast, and uptake variation through a postcode lottery.

Interviews revealed a strong consensus that R&D would be the primary activity impacted by changes in the access environment. Based on the responses provided, three quantitative scenarios have been developed. The middle scenario is based on the median response provided; the low and high scenarios are based on the 25th and 75th percentile responses respectively.

**Figure 35: Access scenarios – potential impact on number of R&D jobs in pharmaceutical manufacturers after five years**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Increased access</th>
<th>Decreased access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low scenario (25th percentile)</td>
<td>5%</td>
<td>-3%</td>
</tr>
<tr>
<td>Middle scenario (median)</td>
<td>8%</td>
<td>-15%</td>
</tr>
<tr>
<td>High scenario (75th percentile)</td>
<td>15%</td>
<td>-30%</td>
</tr>
</tbody>
</table>

Sources: PwC Strategy& analysis, PwC Strategy& interviews, Feb. 2017

The responses were asymmetrical, with a far greater range of impact expected in the decreased access scenario. Some respondents felt that a further deterioration in the access environment could lead to a tipping point: where some companies may relocate all R&D activity out of the UK.

Under the increased access scenario, respondents considered that an increase in UK R&D of between 5% and 15% could be realised.
To estimate how these results could translate to the wider economy, a baseline was used for the current size of the pharmaceutical sector. The baseline was sourced from analysis produced for the ABPI\textsuperscript{44}, estimating that UK pharmaceutical companies:

- Supported £9.6bn in direct GVA in 2015, and a further £6.1bn in multiplier effects;
- Employed 71,000 people in the UK and supported a further 241,000 jobs through the supply chain and economy; and
- Contributed £4.1bn in tax payments to the UK Exchequer

Not all of this activity relates to R&D so based on interviews and with public data released from major UK pharmaceutical companies, one-third of the direct impacts were attributed to R&D based activities.

4.2 The potential economic impact of improved patient access to medicines

By combining the figures set out above, an estimate of the potential economic contribution of improving patient access to medicines was derived.

This analysis considers the direct effect arising from pharmaceutical R&D activities and also the indirect and induced effects of the supply chain and economy - explained below.

- **The direct contribution** – the economic value and employment of pharmaceutical companies themselves;
- **The indirect contribution** – the economic contribution and employment from the supply-chain which arises as pharmaceutical companies purchase goods and services from UK-based suppliers. This channel also considers that not all R&D is conducted in-house and may be contracted out to external companies like Contract Research Organisations (CROs);
- **The induced contribution** – the economic contribution of spending by employees of pharmaceutical companies and their suppliers and contractors on goods and services for their own consumption. For example, this captures the effect of pharmaceutical companies’ employees spending their wages at restaurants in the UK

4.2.1 Impact on jobs

Figure 36: Estimate of economic impact of improved access in terms of UK direct R&D jobs, indirect and induced effects

Sources: PwC Strategy\& analysis, PwC Strategy\& interviews, Feb. 2017

For employment, a boost of more than 4,000 jobs is estimated from improved access in the middle scenario. This comprises of direct employment of 1,900, indirect employment of 1,300 and induced employment of 800 jobs. The low scenario estimate of employment equates to 2,500 jobs in total, increasing to 7,400 in total, in the high scenario estimate.

4.2.2 Impact on Gross Value Added (GVA)

Figure 37: Estimate of economic impact of improved access in terms of GVA increase from direct R&D jobs, indirect and induced effects, 2015 constant prices

Increasing access could boost GVA by £705m each year in the middle scenario estimate. This could range from £435m in the low scenario estimate to £1.3bn in the high scenario estimate.

4.2.3 Impact on the Exchequer

Part of the GVA contribution measured comes in the form of tax receipts to UK Government. It is estimated that the increased access scenario could result in an increase in tax payments of £147m to £442m, with the middle scenario estimate being an increase to £244m.

In the UK, around 20% of public sector expenditure goes to the NHS, meaning a large proportion of this would flow back into the UK healthcare system.

Figure 38: Potential change in tax receipts due to increased access, 2015 constant prices

<table>
<thead>
<tr>
<th>Change in tax receipts relative to baseline after 5 years (£m)</th>
<th>Direct</th>
<th>Indirect &amp; induced</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low scenario</td>
<td>50</td>
<td>97</td>
<td>147</td>
</tr>
<tr>
<td>Middle scenario</td>
<td>83</td>
<td>161</td>
<td>244</td>
</tr>
<tr>
<td>High scenario</td>
<td>151</td>
<td>291</td>
<td>442</td>
</tr>
</tbody>
</table>

Source: PwC Strategy& analysis

4.2.4 Wider impacts on patients, the NHS and welfare

Improving patient access to medicines could have many more benefits, which have not been quantified here.

- **Health benefits**: Patients benefit from earlier and wider access to potentially lifesaving or life enhancing medicines, improving health and quality of life. A greater number of UK clinical trials enable UK patients to access new treatments that would otherwise not be available to them.
- **NHS savings**: The NHS benefits financially from UK clinical trials. Pharmaceutical companies fund the treatment of patients on trials, a cost that would otherwise be borne by the NHS. In addition, the NHS receives fees for conducting trials. The NHS could also make indirect monetary benefits as improved access to newer medicines may improve patient health, potentially reducing the need for future treatment.
- **Welfare effects**: Improved health of the UK population could reduce absences from work, boosting the economy. This may have further knock on effects on the Government welfare bill as improved health reduces the number of people claiming out of work and disability related benefits.

4.2.5 Conclusion

This analysis has estimated the economic impact of improving access in terms of R&D. Improving access to medicines could also positively impact jobs and investment in other pharmaceutical company functions such as commercial teams. Many companies discussed the potential challenges and opportunities associated with Brexit which creates uncertainty, making access important for UK competitiveness.

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45 Source: HMT Public Expenditure Statistical Analyses (PESA)
Chapter 5 – How do we close the access gap in order to maintain an internationally competitive life sciences ecosystem that delivers health and wealth for the UK?
Recognising NHS strengths and cost containment challenges, this analysis has identified opportunities for collaboration across the health system and industry to improve both access to new medicines whilst supporting cost containment, by agreeing an aspiration to reduce the access gap and exploring approaches such as innovative pricing models.

5.1 Next steps

The UK aims to become a globally-unique and internationally competitive life sciences ecosystem that delivers health and wealth and supports NHS transformation. To achieve this, a competitive ecosystem is needed across all factors. It is important to maintain leadership in areas such as science and skills, (particularly in the context of the challenges and opportunities created by the Brexit referendum), to become more competitive on clinical trials infrastructure, digital & data (e.g. RWE), and funding & investment and finally, to improve access to new medicines.

Narrowing the access gap could drive UK life sciences competitiveness, boost UK R&D jobs and stimulate UK science, skills and clinical trial activities. Also, this could revise the current situation where the UK has a strong record in developing the world’s medicines, but patients access up to 75% less new medicines (by volume per capita) compared to other benchmarked countries.

However, this report recognises the broader context of NHS challenges, the need for cost containment and the unique strengths of the NHS. New approaches involving the Government, NHS and industry are needed. Industry is currently a partner in managing healthcare expenditure through a voluntary agreement with the Government to cap the total new medicines bill (which offers a rebate on expenditure exceeding it), yet the benefits are not currently felt within the NHS.

5.1.1 Collaboration to deliver against a shared aspiration

This analysis has identified an opportunity for the UK life sciences and health sectors to agree an aspiration to reduce the access gap. For example, that, by 2021, patient access to new medicines in the UK is broadly in line with comparable countries (such as France and Germany), based on GDP per capita, population and health system dynamics. By setting out a shared aspiration that prioritises patients’ needs, welfare and access to the latest pharmaceutical innovations, senior Ministerial, industry and NHS leadership, can meet regularly to track progress towards this shared goal.

Case study Belgium “Pact of the Future”:

The Pact was signed by the Belgian Minister of Health and the General Association of the Pharmaceutical Industry in July 2015. The Pact forms the basis for a continued open dialogue between the industry, Government and wider stakeholders. Within this, quarterly dialogues are scheduled between the industry and the Minister and Cabinet, to monitor the Pact’s implementation. The Pact endeavoured to offer a medium-to-long term vision that prioritises patients’ needs, welfare and access to the latest pharmaceutical innovations. Its four themes are:

1. Accelerated access for patients to innovative medicines
2. Improved predictability in the funding of a sustainable healthcare system
3. A strengthening of Belgium’s leadership in research and development
4. Enhanced transparency in the interaction between industry and stakeholders

Source: Pfizer internal document. Data on file
5.1.2 Areas to explore

Stakeholders also called for a wide-ranging new approach to access and uptake that goes far beyond current UK plans to implement the Accelerated Access Review.

“The NHS has just built a whole infrastructure aimed at slowing down uptake of new innovation, seeing it as a cost driver and finding any way to slow it down. I think that needs sweeping away.”

Global Biotech

Potential approaches which have been suggested by stakeholders and seen in other leading markets could be further explored.

Implementing innovative pricing models: In these models a company is paid by the NHS only when the drug or therapy achieves a specified outcome e.g. a clinical response to the therapy, improved adherence, or a reduction in A&E admissions. These models enable the health system to deliver outcomes and achieve greater cost effectiveness.

“Our [innovative contracting model] was approved by the trust board 6 times before it ultimately got approval. It eventually got approved because conceptually it was exactly the same deal as the car park they recently built.”

Small Biotech

“If we want to put an innovative scheme to the NHS, [that is] good for patients for access and uptake, I don’t know where in the NHS I can engage that.”

Global Biotech

In some cases facilitating health system stakeholders from the Department of Health, NICE and NHS England to work together to develop a better overall commercial arrangement, and enabling the NHS to transform services with new innovation in consultation with health care professionals and patients, could offer savings.

Furthermore, multi-year budgets would enable the NHS to invest in a therapy in year one, when a saving may only be delivered in years two or three.

Better integration across different budgets and organisations would allow net savings to be realised, where currently perverse incentives lead to greater overall NHS spending as additional spend is required in one budget e.g. spend on new therapies, but a more significant saving is realised elsewhere.

“The system is essentially fragmented, so the part that pays for the pathway doesn’t see the benefits [of savings generated in other areas]. The fragmented clinical pathway certainly prevents drugs from being adopted.”

Academic

5.2 Concluding remarks

This report aims to provide a useful basis for further discussions on how the UK’s successful life sciences sector can continue to drive health and wealth into the future.

Appendix A: Publications used in literature review

Reports are ordered alphabetically by author

ABPI (2014) International Comparison of Medicines Usage

ABPI (2015) Bridging the Skills Gap in the Biopharmaceutical Industry

ABPI, BioIndustry Association, BIA (2016) Maintaining and Growing the UK’s World Leading Life Sciences Sector in the Context of Leaving the EU

Accelerated Access Review, Hugh Taylor (Chair) independent report (2016), Accelerated Access Review


Clarivate Analytics, for the ABPI (2016) Open for Innovation: UK Biopharma R&D Sourcebook 2016

Department of Business, Energy & Industrial Strategy UK Life Sciences Industrial Strategy: Initial Findings (Version 4.0, December 2016)


Lord Sainsbury of Turville (1999) Biotechnology Clusters


NERA, for the Association of the British Pharmaceutical Industry, ABPI (2007) Key Factors in Attracting Internationally Mobile Investments by the Research-Based Pharmaceutical Industry


Publicis Healthcare Consulting, for the European Federation of Pharmaceutical Industries and Associations, EFPIA (2014) Europe Attractiveness in International Clinical Research

PwC Strategy&, for the European Commission (2011) Regional Biotechnology

PwC Strategy&, confidential internal analysis on innovative funding for life sciences R&D (2016)

TBR and CBSL, for the ABPI (2016) The Changing UK Drug Discovery Landscape


UK Science and Technology Select Committee (2013) Bridging the Valley of Death: Improving the Commercialisation of Research
## Appendix B: Organisations interviewed

### B.1 List of organisations interviewed as part of this report

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Type</th>
<th>Other Organisation</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbbVie Inc.</td>
<td>P</td>
<td>F. Hoffman-La Roche AG</td>
<td>P</td>
</tr>
<tr>
<td>Association of the British Pharmaceutical Industry</td>
<td>O</td>
<td>London Stock Exchange Group PLC</td>
<td>O</td>
</tr>
<tr>
<td>Alzheimer’s Research UK</td>
<td>O</td>
<td>MedCity Ltd</td>
<td>O</td>
</tr>
<tr>
<td>Amgen Ltd</td>
<td>P</td>
<td>Merck Sharp &amp; Dohme Ltd</td>
<td>P</td>
</tr>
<tr>
<td>AstraZeneca PLC</td>
<td>P</td>
<td>Northern Health Science Alliance Ltd</td>
<td>O</td>
</tr>
<tr>
<td>Bayer AG</td>
<td>P</td>
<td>Novartis AG</td>
<td>P</td>
</tr>
<tr>
<td>BioIndustry Association</td>
<td>O</td>
<td>Pfizer Inc.</td>
<td>P</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>P</td>
<td>Redx Pharma PLC</td>
<td>B</td>
</tr>
<tr>
<td>Cambridge Enterprise, University of Cambridge</td>
<td>O</td>
<td>Shire PLC</td>
<td>P</td>
</tr>
<tr>
<td>Celgene Corporation</td>
<td>P</td>
<td>Touchstone Innovations PLC</td>
<td>O</td>
</tr>
<tr>
<td>CVC Capital Partners Ltd</td>
<td>O</td>
<td>UCB</td>
<td>P</td>
</tr>
<tr>
<td>Gilead Sciences Inc.</td>
<td>P</td>
<td>UCLPartners Ltd</td>
<td>A</td>
</tr>
<tr>
<td>GlaxoSmithKline PLC</td>
<td>P</td>
<td>University of Manchester</td>
<td>A</td>
</tr>
<tr>
<td>Immunocore Ltd</td>
<td>B</td>
<td>University of Oxford</td>
<td>A</td>
</tr>
<tr>
<td>Eli Lilly and Company</td>
<td>P</td>
<td>Other (1)</td>
<td>O</td>
</tr>
</tbody>
</table>

Key: P = Pharmaceutical and global biotechnology company, B = Small biotechnology company, A = Academia, O = Other

In three cases, more than one person from each organisation was interviewed

### B.2 Roles of individuals interviewed as part of this report

Total number of individuals interviewed: 33

![Pie chart showing roles of individuals interviewed: UK General Manager (Pharmaceutical Company) 41%, CEO / Managing Director (Non-Pharmaceutical Company) 26%, Academic 9%, Other 24%]

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48 Individual has multiple roles within the health sector and participated in an independent capacity
49 ‘Other’ includes roles such as Head of Corporate Affairs, Head of Commercial, Medical Director, CIO etc.
### Appendix C: Benchmarking data tables

#### C.1 Science, innovation and scale

<table>
<thead>
<tr>
<th>Factor</th>
<th>Defined Benchmark</th>
<th>FR</th>
<th>DE</th>
<th>JP</th>
<th>SG</th>
<th>CH</th>
<th>US</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Academic &amp; leading edge science</strong></td>
<td># Life sciences publications per million pop. (2015)(^{50})</td>
<td>57</td>
<td>66</td>
<td>99</td>
<td>197</td>
<td>121</td>
<td>185</td>
<td></td>
</tr>
<tr>
<td></td>
<td># Top 100 global universities for life sciences (2015)(^{51})</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>35</td>
<td>15</td>
</tr>
<tr>
<td><strong>Workforce &amp; skills</strong></td>
<td># New PHDs in science, maths and computing per million pop. (2014)(^{52})</td>
<td>97.3</td>
<td>110.8</td>
<td>19.0</td>
<td>142.5</td>
<td>56.3</td>
<td>125.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td># Researchers in R&amp;D per million pop. (2015)(^{53})</td>
<td>4073.4</td>
<td>4379.1</td>
<td>5083.7</td>
<td>6442.3</td>
<td>4481.1</td>
<td>4018.6</td>
<td>4029.3</td>
</tr>
<tr>
<td><strong>International &amp; regional collaborations</strong></td>
<td># Biotech firms per million pop. (2014 or latest available year)(^{54})</td>
<td>29.3</td>
<td>9.0</td>
<td>4.3</td>
<td>28.5</td>
<td>36.2</td>
<td>7.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td># Life sciences clusters / regions(^{55})</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td><strong>Large pharmaceutical company presence</strong></td>
<td># Global / European HQs for top 20 Pharmaceutical companies(^{56})</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td># R&amp;D sites for top 20 Pharmaceutical companies(^{57})</td>
<td>10</td>
<td>14</td>
<td>14</td>
<td>5</td>
<td>7</td>
<td>71</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td># FDA manufacturing sites for top 20 Pharmaceutical companies(^{58})</td>
<td>27</td>
<td>29</td>
<td>10</td>
<td>14</td>
<td>11</td>
<td>163</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical exports as a % of GDP (2015)(^{59})</td>
<td>1.3</td>
<td>2.3</td>
<td>0.1</td>
<td>2.6</td>
<td>9.7</td>
<td>0.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

**Key:** Data unavailable

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\(^{50}\) UK Life Sciences Industrial Strategy: Initial Findings (2016)

\(^{51}\) QS World University Rankings, (2016/17)

\(^{52}\) OECD Key Biotechnology Indicators (2014)

\(^{53}\) World Bank World Development Indicators (2015)

\(^{54}\) OECD Key Biotechnology Indicators (2014)

\(^{55}\) JLL Life Sciences Cluster Report (2014)

\(^{56}\) Individual Pharmaceutical company websites (2017)

\(^{57}\) Individual Pharmaceutical company websites (2017)

\(^{58}\) EvaluatePharma, PwC Strategy & analysis. Data on file

\(^{59}\) World Trade Organisation, World Bank (2015)
C.2 Economic and political environment

<table>
<thead>
<tr>
<th>Factor</th>
<th>Defined Benchmark</th>
<th>FR</th>
<th>DE</th>
<th>JP</th>
<th>SG</th>
<th>CH</th>
<th>US</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding &amp; investment</td>
<td>Investment from venture financing ($ per capita, 2016)</td>
<td>2.2</td>
<td>2.8</td>
<td>0.2</td>
<td>35.1</td>
<td>21.2</td>
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<td></td>
<td>Industry spend on life sciences R&amp;D ($ per capita, 2015)</td>
<td>85</td>
<td>100</td>
<td>180</td>
<td>480</td>
<td>240</td>
<td>120</td>
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<td></td>
<td>Public spend on life sciences R&amp;D ($ per capita, 2015)</td>
<td>95</td>
<td>90</td>
<td>430</td>
<td>250</td>
<td>100</td>
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<td>Fiscal incentives</td>
<td>Overall tax attractiveness</td>
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<td></td>
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<tr>
<td>Infrastructure e.g.</td>
<td>Quality of overall infrastructure</td>
<td>6.0</td>
<td>5.7</td>
<td>6.2</td>
<td>6.4</td>
<td>6.5</td>
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<tr>
<td>transport and facilities</td>
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Key: Data unavailable

C.3 Health and commercial

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<th>FR</th>
<th>DE</th>
<th>JP</th>
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<th>US</th>
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<tr>
<td>Clinical trials infrastructure</td>
<td># Phase I clinical trials per million pop. (2016)</td>
<td>1.1</td>
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<td># Phase II clinical trials per million pop. (2016)</td>
<td>3.4</td>
<td>2.4</td>
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<tr>
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<td># Phase III clinical trials per million pop. (2016)</td>
<td>3.7</td>
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<td>5.4</td>
<td>2.1</td>
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<tr>
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<td>Phase I # patients enrolled per million pop. (2016)</td>
<td>74.5</td>
<td>63.2</td>
<td>15.3</td>
<td>253.5</td>
<td>101.4</td>
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<td>Phase II # patients enrolled per million pop. (2016)</td>
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<td>355.4</td>
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<td>436.3</td>
<td>1068.3</td>
<td>585.3</td>
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<td>Phase III # patients enrolled per million pop. (2016)</td>
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<td>1509.9</td>
<td>642.3</td>
<td>2484.4</td>
<td>3863.8</td>
<td>1253.8</td>
<td>1669.5</td>
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<td>Phase I, average # patients per trial</td>
<td>69.1</td>
<td>49.5</td>
<td>36.8</td>
<td>73.8</td>
<td>36.5</td>
<td>57.5</td>
<td>51.8</td>
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<td>Phase II, average # patients per trial</td>
<td>134.1</td>
<td>146.1</td>
<td>152.3</td>
<td>115.0</td>
<td>177.1</td>
<td>121.3</td>
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<td>Phase III, average # patients per trial</td>
<td>484.5</td>
<td>668.1</td>
<td>622.5</td>
<td>916.7</td>
<td>711.5</td>
<td>593.5</td>
<td>799.6</td>
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60 EvaluatePharma, PwC Strategy & analysis. Data on file
63 PwC World Wide Tax Summaries, PwC Tax experts’ analysis, overall tax attractiveness analysed based on the statutory tax rate, IP regimes, and R&D / manufacturing incentives available in each country. Rating based on R/A/G scale, green representing the best tax incentives. Data provided by PwC Tax experts. Data on file
64 WEF Global Competitiveness Report (2016-17)
65 All indicators up to and including “Phase III, average # patients per trial” was sourced from Clinicaltrials.gov, trials first received in 2016
<table>
<thead>
<tr>
<th>Factor</th>
<th>Defined Benchmark</th>
<th>FR</th>
<th>DE</th>
<th>JP</th>
<th>SG</th>
<th>CH</th>
<th>US</th>
<th>UK</th>
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<td>Index median cost per visit</td>
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<td>58</td>
<td>87</td>
<td>114</td>
<td>145</td>
<td>100</td>
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<tr>
<td>Digital &amp; data</td>
<td>Connected-care technology adoption sub-index</td>
<td>42.6</td>
<td>41.5</td>
<td>38.4</td>
<td>48.2</td>
<td></td>
<td>49</td>
<td>45.3</td>
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<tr>
<td></td>
<td>Ease and value of data</td>
<td>69</td>
<td>85</td>
<td>83</td>
<td></td>
<td>100</td>
<td>74</td>
<td></td>
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<tr>
<td>Patient access to medicines</td>
<td>Volume uptake, # standard units purchased in Y1 post-launch, per '000 pop. (2011 – 2016)</td>
<td>1271.6</td>
<td>1765.3</td>
<td>794.8</td>
<td>1699.3</td>
<td>921.0</td>
<td>370.4</td>
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</table>

Key: Data unavailable

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67 Future Health Index (2016)
68 This is a weighting factor based on insight from PwC Strategy& experts on the ease of accessing data and the value of data to the benchmarked country
69 QuintilesIMS. (2017) Data on file
## Appendix D: Basket of 76 products analysed in Chapter 3

<table>
<thead>
<tr>
<th>Product</th>
<th>EMA Indication(s)</th>
<th>Disease Area</th>
<th>US FDA CDER Novel Drug?</th>
<th>NICE Decision</th>
<th>Markets with no sales data</th>
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</thead>
<tbody>
<tr>
<td>ADCETRIS</td>
<td>Cancer – Hodgkin’s lymphoma (HL), systemic anaplastic large cell lymphoma (sALCL)</td>
<td>Oncology</td>
<td>Y</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>ADEMPAS</td>
<td>Chronic thromboembolic pulmonary hypertension (CTEPH), pulmonary arterial hypertension (PAH)</td>
<td>Cardiovascular</td>
<td>Y</td>
<td>N/A</td>
<td></td>
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<tr>
<td>AUBAGIO</td>
<td>Multiple sclerosis (MS)</td>
<td>Neurology</td>
<td></td>
<td>Recommended for MS</td>
<td>Japan</td>
</tr>
<tr>
<td>BENLYSTA</td>
<td>Systemic lupus erythematosus (SLE)</td>
<td>Immunology &amp; inflammation and ocular</td>
<td>Y</td>
<td>Recommended for Lupus</td>
<td>Japan</td>
</tr>
<tr>
<td>BETANIS / BETMIGA / MYRBETRIQ</td>
<td>Overactive bladder syndrome</td>
<td>Miscellaneous</td>
<td></td>
<td>Recommended for overactive bladder</td>
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<tr>
<td>BOSULIF</td>
<td>Cancer - chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), pancreatic etc.</td>
<td>Oncology</td>
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<td>Recommended for CML</td>
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<tr>
<td>CAPRELSA</td>
<td>Cancer – thyroid</td>
<td>Oncology</td>
<td>Y</td>
<td>N/A</td>
<td>US</td>
</tr>
<tr>
<td>COMPLERA / EVIPLERA</td>
<td>HIV</td>
<td>Infectious diseases</td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>COSENTYX</td>
<td>Plaque psoriasis, psoriatic arthritis, ankylosing spondylitis</td>
<td>Immunology &amp; inflammation and ocular</td>
<td></td>
<td>Recommended for plaque psoriasis, ankylosing spondylitis</td>
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<tr>
<td>COTELLIC</td>
<td>Cancer – melanoma</td>
<td>Oncology</td>
<td>Y</td>
<td>Not recommended</td>
<td>Japan</td>
</tr>
<tr>
<td>CYRAMZA</td>
<td>Cancer – stomach, gastro-esophageal junction adenocarcinoma, metastatic colorectal, non-small cell lung (NSCLC)</td>
<td>Oncology</td>
<td>Y</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>DAKLINZA</td>
<td>Hepatitis C</td>
<td>Infectious diseases</td>
<td>Y</td>
<td>N/A</td>
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<tr>
<td>DEXDOR</td>
<td>Intensive care sedation</td>
<td>Miscellaneous</td>
<td></td>
<td>N/A</td>
<td>Japan, Switzerland</td>
</tr>
<tr>
<td>DIFICID / DIFICLIR</td>
<td>Clostridium difficile-associated diarrhoea (CDAD)</td>
<td>Infectious diseases</td>
<td>Y</td>
<td>N/A</td>
<td>Japan</td>
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<tr>
<td>EDURANT</td>
<td>HIV</td>
<td>Infectious diseases</td>
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<td>N/A</td>
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<tr>
<td>ELIQUIS</td>
<td>Venous thromboembolism, Deep Vein Thrombosis (DVT), pulmonary embolism, stroke /blood clot prevention in adults with atrial fibrillation</td>
<td>Cardiovascular</td>
<td>Y</td>
<td>Recommended for DVT, pulmonary embolism, preventing stroke, systemic embolism</td>
<td></td>
</tr>
<tr>
<td>Product</td>
<td>EMA Indication(s)</td>
<td>Disease Area</td>
<td>US FDA CDER Novel Drug?</td>
<td>NICE Decision</td>
<td>Markets with no sales data</td>
</tr>
<tr>
<td>-----------------</td>
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<td>---------------------------------------------------</td>
<td>-------------------------</td>
<td>--------------------------------</td>
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<tr>
<td>ENTYVIO</td>
<td>Ulcerative colitis, Crohn’s</td>
<td>Immunology &amp; inflammation and ocular</td>
<td>Y</td>
<td>Recommended for ulcerative colitis, optimized for Crohn’s</td>
<td>Japan</td>
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<tr>
<td>ERIVEDGE</td>
<td>Cancer - basal cell carcinoma (BCC)</td>
<td>Oncology</td>
<td>Y</td>
<td>N/A</td>
<td>Japan</td>
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<tr>
<td>ESBRIET</td>
<td>Idiopathic pulmonary fibrosis (IPF)</td>
<td>Respiratory</td>
<td>Y</td>
<td>Optimised for idiopathic pulmonary fibrosis</td>
<td>Japan</td>
</tr>
<tr>
<td>EYLEA</td>
<td>Wet AMD, macular oedema, diabetic macular oedema, myopic choroidal neovascularisation</td>
<td>Immunology &amp; inflammation and ocular</td>
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<td>Recommended for wet AMD, diabetic macular oedema</td>
<td>Japan</td>
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<tr>
<td>FARYDAK</td>
<td>Cancer – multiple myeloma</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for myeloma</td>
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</tr>
<tr>
<td>FORXIGA / FARXIGA</td>
<td>Diabetes – type 2</td>
<td>Metabolic</td>
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<td>Recommended for type 2 diabetes in combination, optimised as monotherapy</td>
<td>France</td>
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<tr>
<td>FYCOMPA</td>
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<td>GAZYVA</td>
<td>Cancer – CLL, follicular lymphoma (FL)</td>
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<td>GIOTRIF</td>
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<td>Y</td>
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<td>HARVONI</td>
<td>Hepatitis C</td>
<td>Infectious diseases</td>
<td>Y</td>
<td>Optimised for Hepatitis C genotypes 1 and 4</td>
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<td>ICLUSIG</td>
<td>Cancer – CML, ALL</td>
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<td>N/A</td>
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<td>IMBRUVICA</td>
<td>Cancer – NHL, CLL, Waldenström’s macroglobulinaemia etc.</td>
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<td>Recommended for RCC</td>
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<td>INVOKANA</td>
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<td>France, Japan</td>
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<tr>
<td>JAKAVI / JAKAFI</td>
<td>Myelofibrosis, polycythaemia vera</td>
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<td>Optimised for disease-related splenomegaly or symptoms in adults with myelofibrosis</td>
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<tr>
<td>KADCYLA</td>
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<td>KALYDECO</td>
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<sup>70</sup> Kadcyla has been available to UK patients via the Cancer Drugs Fund
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<tr>
<th>Product</th>
<th>EMA Indication(s)</th>
<th>Disease Area</th>
<th>US FDA CDER Novel Drug?</th>
<th>NICE Decision</th>
<th>Markets with no sales data</th>
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<td>LENVIMA</td>
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<td>Stroke prevention, systemic embolism, DVT</td>
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<td>LYNPARZA</td>
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<td>IPF</td>
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<td>Japan</td>
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<tr>
<td>POMALYST / IMNOVID</td>
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<td>Oncology</td>
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<td>Optimised for myeloma</td>
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<td>SELINCRO</td>
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<td>SIGNIFOR</td>
<td>Cancer – Cushing's disease, acromegaly</td>
<td>Oncology</td>
<td>N/A</td>
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<td>Japan</td>
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<td>SOVALDI</td>
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<td>Infectious diseases</td>
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<td>Optimised for Hepatitis C, genotypes 1, 2, 3, 4, 5, 6</td>
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<td>Recommended for Hepatitis C, genotypes 1 and 4</td>
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<tr>
<td>Product</td>
<td>EMA Indication(s)</td>
<td>Disease Area</td>
<td>US FDA CDER Novel Drug?</td>
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<td>STIVARGA</td>
<td>Cancer – colorectal, gastro-intestinal stromal tumours (GIST)</td>
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<td>N/A</td>
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<td>STRIBILD</td>
<td>HIV</td>
<td>Infectious diseases</td>
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<td>Recommended for melanoma</td>
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<tr>
<td>TECFIDERA</td>
<td>MS</td>
<td>Neurology</td>
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<td>Recommended for MS</td>
<td>Japan</td>
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<tr>
<td>TRAJENTA / TRAJECTA</td>
<td>Diabetes – type 2</td>
<td>Metabolic</td>
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<tr>
<td>TRESIBA</td>
<td>Diabetes – type 1, 2</td>
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<td>HIV</td>
<td>Infectious diseases</td>
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<td>Neurology</td>
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<td>Recommended for epilepsy</td>
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<td>VICTRELIS</td>
<td>Hepatitis C</td>
<td>Infectious diseases</td>
<td>Y</td>
<td>Recommended for Hepatitis C, genotype 1</td>
<td>Japan</td>
</tr>
<tr>
<td>VIEKIRA PAK / VIEKIRAX</td>
<td>Hepatitis C</td>
<td>Infectious diseases</td>
<td>Y</td>
<td>Recommended for Hepatitis C, genotype 1</td>
<td></td>
</tr>
<tr>
<td>VIMIZIM</td>
<td>Mucopolysaccharidosis type IVA</td>
<td>Metabolic</td>
<td>Y</td>
<td>Recommended for mucopolysaccharidosis type IVA</td>
<td>Switzerland</td>
</tr>
<tr>
<td>VYNDAGEL</td>
<td>Transthyretin amyloidosis</td>
<td>Neurology</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XALKORI</td>
<td>Cancer – NSCLC</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for NSCLC</td>
<td></td>
</tr>
<tr>
<td>XTANDI</td>
<td>Cancer – prostate</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for prostate cancer</td>
<td></td>
</tr>
<tr>
<td>YELLOX</td>
<td>Ocular inflammation post-cataract removal</td>
<td>Immunology &amp; inflammation and ocular</td>
<td>N/A</td>
<td></td>
<td>Japan, US</td>
</tr>
<tr>
<td>YERVOY</td>
<td>Cancer – melanoma</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for melanoma</td>
<td></td>
</tr>
<tr>
<td>ZALTRAP</td>
<td>Cancer – metastatic colorectal</td>
<td>Oncology</td>
<td>Y</td>
<td>Not recommended</td>
<td>Japan</td>
</tr>
<tr>
<td>ZELBORAF</td>
<td>Cancer – melanoma</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for melanoma</td>
<td></td>
</tr>
<tr>
<td>ZOELY</td>
<td>Female contraception</td>
<td>Miscellaneous</td>
<td>N/A</td>
<td></td>
<td>Japan, US</td>
</tr>
<tr>
<td>ZYDELIG</td>
<td>Cancer – CLL, follicular lymphoma</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for CLL</td>
<td>Japan</td>
</tr>
<tr>
<td>ZYKADIA</td>
<td>Cancer – NSCLC</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for NSCLC</td>
<td>Switzerland</td>
</tr>
<tr>
<td>ZYTIGA</td>
<td>Cancer – prostate</td>
<td>Oncology</td>
<td>Y</td>
<td>Recommended for prostate cancer</td>
<td></td>
</tr>
</tbody>
</table>
Appendix E: Additional methodology for analysis in Chapter 3

E.1 Standard Units
The analysis in Chapter 3 is based on sales volumes data given in standard units. The data was provided by QuintilesIMS. Standard Units are the smallest common dose of a product formulation and are more appropriate when comparing sales of products with different formulations.

E.2 Conversion to ‘per million population’ (pmp)
The data from QuintilesIMS was provided quarterly by product and by country, e.g. Q1 2016 sales volumes for Zytiga in the UK were 1.01 million standard units. To make this comparable across the benchmarked countries, this was adjusted to a per million population (pmp) figure using the populations for each country and year respectively. The population statistics were sourced from the World Bank.

E.3 Normalisation of launch years
In order to normalise launch years, the first four quarters post-launch were taken to be the ‘first year’. Specifically, the first quarter to have any sales data is considered to be ‘Q1’ of the ‘first year’, with the subsequent three quarters making up ‘Q2’, ‘Q3’ and ‘Q4’ respectively. This methodology was chosen in order to measure the immediate uptake of new products post-launch. However, it should be noted that as a result, there is some variation between countries as ‘Q1’ covers different durations.

To address this issue, a sensitivity analysis was conducted to compare the impact of using the first four quarters of data (Method 1) against using the first four full quarters (Method 2). Method 2 was shown to impact UK data points more than the other benchmarked countries, suggesting an over-estimate of the access gap. Method 2 decreased the differential in access between the UK and the average across all benchmarked countries for all 76 products from 75% to 68%. However if Method 2 had been applied, three products would not have met the minimum inclusion criteria of four quarters of data across at least four benchmark countries. It is unclear why the UK is impacted more than other markets by the methodology applied in this analysis. The reason for lower ‘Q1’ sales in the UK has not been analysed within the scope of this report.

E.4 Differences between definitions used in this analysis and by NICE
NICE considers both ‘recommended’ and ‘optimised’ products to be recommended, however where this analysis refers to ‘recommended’ products, it refers to those with a full NICE recommendation only. For example, Figure 23 in Chapter 3 only shows data for products with a full NICE recommendation, and excludes ‘optimised’ products.

By considering ‘optimised’ products to be recommended and including them into the analysis for Figure 23, the differential between the UK and the average across all benchmarked countries increased from 64% to 66%. This is as expected due to optimised products having limited access based on indication, disease severity or stage of treatment.

E.5 Data limitations and potential variations across countries
As the European Medicines Agency regulates France, Germany and the UK, the relative barriers in the access environment do not relate to Market Authorisation. Outside of Europe and beyond the jurisdiction of EMA regulation, medicines may not be launched, may be given marketing authorisation for different indications or even different doses, dependent on the regulatory body concerned. These factors could influence uptake
across geographies. In addition, there may be differences in uptake due to ethnicities in each country, which can impact patient metabolism and drug usage.

In some cases, products will not have launched in one or two countries. The UK is less frequently a non-launch market than others, meaning access in other markets may be underestimated in comparison. Non-launched products by country are UK (1), Germany (1), US (6), Switzerland (7), France (10), and Japan (28).

Further analysis was conducted on a sample of medicines covering 30% of the general basket by volume, 50% of the oncology basket by volume, and 55% of the hepatitis C basket by volume, to check variations in indication and recommended dosage across the EMA and US FDA. These products were chosen as they are most likely to have significant effects on the data due to their larger share of the sample basket. In this sample, c.50% had no variations, and the remainder had only minor differences between the two regulatory bodies. For example, Harvoni (ledipasvir/sofosbuvir) is indicated for an extra genotype of hepatitis C (genotype 3) for some patients by the EMA, and its recommended treatment duration ranges from 8-24 weeks for the EMA compared to 12-24 weeks for the FDA. The differences found in dosing were likely to be negligible over a long period of time. For example, in the case of Betanis (mirabegron), the EMA recommends 50mg once per day, whereas the FDA recommends a starting dose of 25mg, which can then be increased to 50mg.
Executive Summary References

1. ABPI, The economic contribution of the UK Life Sciences industry (2017), p. 15
2. HMT Public Expenditure Statistical Analysis (PESA) 2015-16 Actuals
4. See Appendix B for details of organisations interviewed
5. These stakeholders were asked about R&D only
6. Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals
7. New medicines are defined as patent protected drugs launched from 2011-16. The percentage given applies to all products that fit this category that had at least 1 year of sales data across at least four benchmark countries to allow for access comparisons to be made. Access is measured by volume of drugs in standard units and this is adjusted per million population for each country
8. Products classified by the US Food and Drugs Administration (FDA) as ‘novel’ include those that have been designated for Fast-Track, Breakthrough, Priority Review or Accelerated Approval by the FDA. They are defined as follows ‘Novel drugs are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient care and public health. New molecular entities (NMEs) have chemical structures that have never been approved before. However, in some cases an NME may have actions similar to earlier drugs and may not necessarily offer unique clinical advantages over existing therapies.’ Source: www.fda.gov [accessed 10 Feb. 2017]
10. Standard 90 day requirement in which NHS organisations have to make funding for NICE-recommended treatments available. Source: www.nice.org.uk
12. Pharmaceutical company spending is increased or there is a greater share for Innovative Rx (innovative prescribing), an expanded model of accelerated access is applied similar to FDA Breakthrough Therapy, NICE approval is accelerated to earlier R&D stage (Ph. II) and reimbursement linked to Real World Data and the UK becomes a leader in innovative pricing and rewards innovation