FUTURE OF PHARMACEUTICALS

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FUTURE OF PHARMACEUTICALS

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TECH HUBS

An industry on the move

Pharmaceuticals is changing. Gone are the security gates and perimeter walls as companies move to be part of open, learning communities where collaboration is at the forefront of business

Danny Buckland

The pharmaceutical industry is moving places as real estate becomes a huge factor in drug development and corporate success.

Companies that luxuriated in headquarters secreted behind high walls and security booths are venturing out to take space in science parks and UK tech hubs alongside startups and academic institutions.

The age of isolation has been replaced by integration with executives busily thumbing property brochures to secure the best office and lab space next to the brightest research minds.

Novartis is moving its UK base from the Surrey countryside to White City Place, the redeveloped BBC Television Centre site, to be in the midst of Imperial College London's research campus, while MSD is viewing potential plots in the heart of the capital for a new Discovery Centre and HQ, ready to leave its current Hertfordshire base.

AstraZeneca has invested £500 million on a new headquarters at the Cambridge Biomedical Campus, one of the premier UK tech hubs which spans 170 acres to the south of the city and is home to life science heavy hitters and sparky startups.

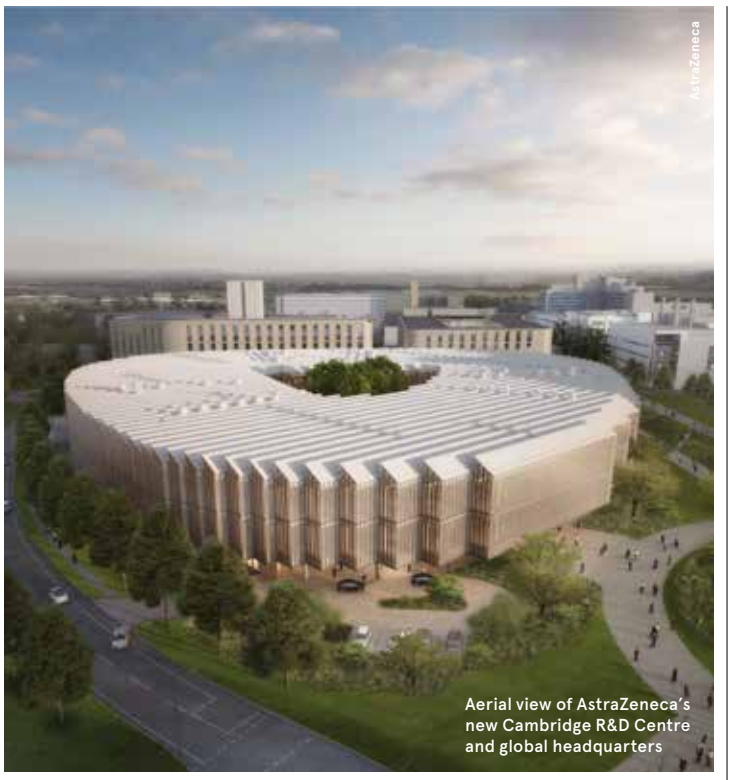
The statement building, with courtyards referencing nearby colleges, has been designed to be open and collaborative with no whiff of forbidding entry gates or turnstiles. It even has a café open to the public and outreach is high on the menu.

"It is a radical transformation. Property and real estate, which was an operational necessity, is moving to being a strategic imperative," says Dr Glen Crocker, head of life sciences at property advisers JLL. "Where you are, who you are located next to matters now, particularly in terms of attracting a younger generation of talent.

"The AstraZeneca building has an open design, inviting people in, whereas if you went to its former Cheshire base, there would be security gates and barriers.

"We are also seeing a lot more multi-occupancy buildings containing a mix of pharma companies, incubators and university research with common breakout areas and cafés. New buildings are being designed with this in mind, but you have to think about how you curate these spaces to make the best of the collaborative potential."

The main factors are the expense of drug development, blockbuster drugs passing out of lucrative patent phases and the need for innovative approaches to tackle rare diseases. But the sudden wash of venture capital (VC) coming into life sciences – 2018 was a record investment year in the UK and globally – is also compelling pharma to have property agents on speed dial.



Aerial view of AstraZeneca's new Cambridge R&D Centre and global headquarters

"It used to be that early-stage companies were short of cash and had to go cap in hand to pharma companies that could sit back and take their pick," says Dr Crocker. "The balance of power has shifted as the startups now have VC backing and can hang on to their innovative products for longer, so we are seeing pharma revisit how it does business.

"Small companies are responsible for around 70 per cent of biopharma products in development and, if you want access to that and the talent, you have to be there, in the midst of it."

A prime example of a rapidly forming UK tech hub is the Francis Crick Institute, the largest biomedical laboratory in Europe, which has 1,200 scientists under its roof in King's Cross, London, and is also home to outposts of GSK, Novartis and MSD, sharing ideas and staff.

Véronique Birault, Crick director of translation, sums up the appeal: "Collaboration is at the heart of what we do. The Crick was designed to make it as easy as possible for people from all areas to work together.

"Working together with scientists from pharmaceutical companies from an early stage of research helps us build knowledge and understanding from the ground up. By combining our expertise, we hope to truly advance the understanding of complex conditions and potentially offer hope for future generations."

About to rise from a neighbouring site is a 100,000sqft extension to the British Library, which will feature the National Institute for Data Science and Artificial Intelligence, known as the Alan Turing Institute, and prime lab and office space for the booming life sciences sector, predicted to need 1.5 million square feet of extra space over the next five years.

Pharmaceutical companies are now prime players in the property market as they chase new models of drug development and MSD has been working the market hard for the perfect new home.

"We are very excited about the move to central London and the potential it will bring," says Dr Fiona Marshall, head of MSD Discovery Science UK. "We want to be near the people we are going to be collaborating with. Scientific knowledge has more opportunity to advance when people share ideas. We believe the move will be a dynamic shift for innovation and R&D."

Novartis is selling its long-term home in Frimley after moving 550 staff to west London. Haseeb Ahmad, country president Novartis UK, says: "Novartis made the decision to move our UK headquarters to White City to be closer to our key customers, partners and stakeholders, and become better networked in the healthcare and life sciences ecosystem.

"White City is quickly becoming one of the UK's important life sciences and technology districts and we are now at the centre of that, which is very exciting for us and will help us deliver on our ambition to reimagine medicine."

"Golden triangle" cities (London, Cambridge and Oxford) are home to...

39% of UK biological research power

73% of life sciences investment

20% of UK life sciences companies

BioCity/JLL 2019

Analuisa Gamboa/Unsplash

NEW MEDICINES

Can AI help bring new drugs to market?

Early-stage drug development is a critical time, when failure can mean disappointment for patients and runaway costs for companies, but now artificial intelligence can make a difference

Janet Fricker

Introducing artificial intelligence (AI) in the development of new medicines can help to identify drug targets more effectively, cut research and development (R&D) costs and reduce the average time of getting drugs to market.

"AI provides a trail for drug hunters to follow that helps make sense of increasingly complex data sets in medicine," says Chris Molloy, chief executive of Medicines Discovery Catapult.

10-15YRS

the average time of getting drugs to market

Centre for Ageing Better 2019

"In early drug development, the determinants of success are whether you can correctly identify the area of biology that's gone wrong; whether a protein, receptor or a gene, which could then be influenced by introducing a candidate drug."

If investigators can confirm this "drug target" at an early stage using technology such as AI, he adds, they significantly derisk their R&D.

No one doubts new models of drug development are urgently required. A 2018 study, published in the journal *Biostatistics*, which reviewed 21,000 compounds, found around six out of seven potential new drugs fail somewhere between phase-1 trials and regulatory approval.

Furthermore, a 2014 study, published in *Nature Biotech*, showed the costs of failed trials for new medicines range from $800 million to $1.4 billion, and Tufts Center for the Study of Drug Development, in Boston, estimates the average time of getting drugs to market is ten to fifteen years.

In addition to the financial cost of failure, there is the heartache of patients who have no new medicines available. According to Global Genes Allies in Rare Disease, 95 per cent of the 350 million people suffering from rare diseases worldwide have no approved treatments.

A paper published this year by the Institute of Cancer Research agreed there is a huge unmet need which should be addressed with new technology. "An innovation gap or 'valley of death' has opened up between advances in scientific understanding and the clinical and commercial development of new treatments," the report says.

All this is set against an evolving landscape of early-stage drug development. *State of the Discovery Nation 2019*, a joint report by Medicines Discovery Catapult and the BioIndustry Association, found that of the 300 UK companies focused on discovering new medicines, 60 per cent have fewer than five staff members.

"As productivity in big pharma R&D has declined, the role of small and medium-sized enterprises (SMEs) as agile risk takers has increased," says Mr Molloy. The real challenge for small companies with a handful of employees, he adds, is that taking an idea to a commercial reality is a team sport requiring the involvement of more than 100 different specialist disciplines which they need to finance.

For effective drug development, SMEs that typically have funding from seed money and family and friends for around six to twelve months can derive enormous benefits from access to cutting-edge technology.

Access to AI and machine-learning is a game-changer for SMEs, offering the potential to reduce R&D costs and improve drug development efficiency. AI offers a valuable tool for identifying patterns in complex medical datasets and is starting to unlock the potential of decades of medical research.

"It can propose drug targets, design molecules, define the best patients in which to test the molecule to drive greater clinical success and recognise which patients are more likely to experience side effects," says Mark Davies, from BenevolentAI, a company specialising in drug discovery AI.

If the target proves not to be chemically tractable, AI can look further upstream or downstream in the disease pathway for alternative targets open to medicinal chemistry. In late-stage drug development, AI can be used to identify biomarkers used in patient selection, change enrolment criteria and analyse real-world evidence from wearables.

AI in drug development is not science fiction, but is already being used in the here and now. Recently BenevolentAI's computational and experimental platform identified a breast cancer drug as a good candidate for treating motor neurone disease, a condition with considerable unmet medical need, where current treatments only average a three-month extension of life. In a disease model of motor neurone disease, the drug showed promise in delaying the onset of symptoms.

> **AI provides a trail for drug hunters to follow that helps make sense of increasingly complex data sets in medicine**

Model of efficient drug development

Crizotinib (Xalkori), a targeted cancer drug for non-small cell lung cancer (NSCLC), achieved one of the fastest times of drugs to market, with the discovery of the target, an ALK fusion gene. Accelerated US Food and Drug Administration approval took just four years.

Heralded as a model of efficient drug development, this was achieved through effective collaborations between pharmaceutical companies, academic institutes and regulatory agencies.

The first drug development milestone was identification of the ALK fusion protein by Japanese researchers in 2007, when a small minority (around 6 per cent) of NSCLC patients were found to have a fusion gene driving cancer growth.

Serendipitously, discovery of the ALK rearrangement coincided with a parallel drug development programme exploring crizotinib, an agent specially designed to target an entirely different mutation known as MET. In addition to patients with glioblastoma and gastro oesophageal cancer, the MET mutation is also found in some patients with NSCLC.

The focus of the phase-1 trial of crizotinib in MET tumours, which Pfizer had first initiated in 2006, shifted dramatically when significant tumour shrinkage was noted in three out of ten NSCLC patients harbouring ALK rearrangements.

Once the maximum tolerated dose had been identified, investigators had the flexibility to enrol an additional cohort of NSCLC patients with ALK fusion proteins.

"One of the keys to success was the modification of a fluorescence in situ hybridisation, or FISH, probe by clinicians at Massachusetts General Hospital, which was initially designed to detect ALK rearrangement in anaplastic large cell lymphoma. This enabled us to identify in real time NSCLC patients with relevant ALK mutations," says Dr Olivia Ashman, UK oncology medical director at Pfizer.

Of 1,500 NSCLC patients screened, the probe identified 82 ALK positive patients, 47 of whom went on to respond to crizotinib. It was this data that ultimately resulted in accelerated approval being granted for crizotinib in 2011 due to unmet NSCLC need.

A standardised and validated FISH test, developed by Abbott, was co-approved with crizotinib allowing identification of patients most likely to benefit from the new medicine. As a condition of the accelerated approval, further post-marketing testing was required, with crizotinib receiving full approval following phase-3 trial results in 2013.

Tackling the next frontier of liver disease

An innovative pharma company has set its sights on treating non-viral liver diseases

Tackling viral diseases has created landmark advances for the benefit of patients, but scientists and researchers are not pausing to celebrate.

Wrestling control of HIV and hepatitis C has brought hope and health to millions. However, other conditions are now commanding the clinical community's attention, including the rise of non-viral liver diseases and the growth of non-alcoholic steatohepatitis (NASH), in particular.

One of the leading companies addressing this challenge is Intercept Pharmaceuticals. Founded in 2002, after the discovery of the therapeutic potential of bile acid, the company is continuing to prove it is a driving force in the treatment of non-viral liver diseases.

Intercept, based in New York and with international headquarters in London, dedicates its efforts and resources to innovative treatments in non-viral liver diseases where there are little to no options for patients. Its first approved treatment was for primary biliary cholangitis (PBC) where there had been no new treatments approved for 20 years. PBC is a complex condition that mainly affects women and can lead to liver failure.

"We are building a company that has big pharma experience and developmental expertise, while retaining entrepreneurial spirit, and most of all, a company that has people who really understand the science," says Lisa Bright, president, international, at Intercept, whose career includes spells at GSK, Sanofi (then Aventis) and Gilead, before joining Intercept in 2014.

"What we've done at Intercept is quite unique. We have a firm basis in science, led by our founder and chief executive Dr Mark Pruzanski. But unlike many of our peer companies of the same size with a strong clinical focus, we also have the internal capabilities to successfully advance each of our development products from the lab through to commercialisation," says Ms Bright.

The company has grown to more than 500 employees globally and, although small by comparison to some of its potential competitors, it packs a punch. It realised one of the fastest positive opinions from the National Institute for Health and Care Excellence for an orphan medication and has invested almost $1 billion in research and development globally since 2010.

"I have worked in hepatology for a long time and have been involved with hepatitis B and C, and witnessed the great strides forward in treating viral liver disease. Soon these diseases won't be the leading cause of transplantation because of the amazing work that has happened to date," says Ms Bright.

"Intercept appealed to me because it was working in the next area of unmet need in liver disease. We all wanted to continue the journey with the hepatology community whom we'd collaborated with for so many years and were excited by the opportunity to continue to advance the science and to build a new company virtually from scratch."

> **Ultimately, our goal is to stop serious non-viral liver diseases progressing to cirrhosis**

Its main focus now is NASH, a non-viral condition in which the current treatments are primarily limited to lifestyle changes. Its symptoms are often silent, as fat and scarring build-up in the liver consequently leading to fibrosis, potential cirrhosis and the need for a liver transplant.

With NASH prevalence expected to rise 63 per cent by 2030 in the United States, the statistics are daunting and the hepatology community now faces an urgent public health challenge. As early as 2020, NASH is projected to become the leading cause of liver transplants in America, while the British Liver Trust warns the condition will place a huge burden on the NHS in coming years, mostly due to patients in the advanced fibrosis stage of the disease.

"Clinical development in this area is not easy. The science and our understanding of the disease are still evolving and will continue to do so with the growing number of clinical trials in the coming years," says Ms Bright.

Intercept's ongoing clinical trials include REGENERATE, focused on patients with liver fibrosis due to NASH, and REVERSE, focused on patients with compensated cirrhosis due to NASH. The company's new drug application has just been accepted in the United States based on interim results from REGENERATE and the company is planning to file for product approval in the European Union before the end of the year.

"We have been a pioneer in the non-viral liver space and our success to date is a testament to the vision of our founders and the fact that science and community collaboration has remained at the core of what we do," says Ms Bright.

These form part of the reasons why Intercept chose to base its international headquarters in London, which is often selected by businesses because of its proximity to the heart of pharmaceutical research and development in the UK, the south east of England, as well as its connectivity to the rest of the world.

"London has always been a hub for scientific research and development, particularly in liver disease, with a lot of our thought leaders based here. But it's also been such a great hub for industry talent," says Ms Bright.

"We have partnered with hundreds of research sites around the world, funded numerous investigator-initiated and real-world evidence studies and have set up the Practice to Policy Awards programme to fund grassroots innovation in the community. Understanding the science and innovation is critical and really shapes everything we do.

"Ultimately, our goal is to stop serious non-viral liver diseases progressing to cirrhosis. When you realise the terrible consequences cirrhosis can have on a person and their family, it becomes a great motivator to find new solutions for them."

For more information please visit www.interceptpharma.com

UK-NP-N/A-0147. December 2019

Intercept

PHARMA 4.0

Pharma factories feel the pressure to evolve

For an industry which prides itself on being at the cutting edge, pharmaceuticals is lagging behind in exploiting the technological possibilities of Industry 4.0

Martin Barrow

These are challenging times for the pharmaceuticals sector and Pharma 4.0 signals a new way forward.

The era of blockbuster drugs is over and the huge revenues they earned are gone for good. Development costs for a new generation of precision medicines are sky high and only a small number will ever be used to treat patients, which means billions of research-and-development pounds must be written off.

All this is happening at a time when pharmaceutical manufacturing is under greater public scrutiny, facing challenges over efficacy and safety. Meanwhile, public health systems such as the NHS, fighting their own battles to be sustainable, are demanding ever-lower prices for drugs.

Less than a decade ago, the biggest pharmaceutical companies appeared unassailable. Today, investors are not so sure. Although global demand for drugs is growing and the pipeline is more exciting than it has ever been, big pharma is struggling to reinvent itself for the 21st century.

Where pharma once led, it now lags behind other industries in the adoption of Industry 4.0 technologies, which are changing the face of other manufacturing sectors such as aerospace and electronics.

It is being hailed as the fourth industrial revolution and the emerging technologies of Industry 4.0, from digitalisation and automation to advanced analytics and process control, have the potential to transform every aspect of pharmaceutical manufacturing.

According to management consultancy McKinsey & Company, Pharma 4.0 can deliver 30 to 40 per cent improvements in productivity within already mature and efficient lab environments, and a full range of improvements could lead to reductions of more than 50 per cent in overall costs of quality control.

> **Although biopharma has lagged behind industries such as aerospace and electronics, we are learning from others**

Digitalisation and automation will also lead to better quality and compliance by reducing manual errors and variability, as well as allowing faster and more effective resolution of problems.

Pharma 4.0 technology allows for continuous, real-time monitoring of manufacturing processes in smart factories, so any drift away from specified parameters can be predicted and rectified before it turns into a deviation, avoiding the associated downtime and loss of product.

There are examples of Pharma 4.0 driving a 65 per cent reduction in deviations and closure times that are 90 per cent faster. Prevention of major compliance issues can in itself be worth millions in cost-savings. Improved agility and shorter testing time can reduce quality control-lab lead times by 60 to 70 per cent.

Why is Pharma 4.0 not yet embedded in an industry that takes pride in its ability to innovate? Senior managers have struggled to define a clear business case for digitisation or automation. The potential for Pharma 4.0 is so huge, and so broad, that many pharmaceutical companies rushing to adopt the technology have not first paused to consider what they are trying to achieve and what main problems they need to address.

Dr Francisco Leira, executive director for internal and external manufacturing, biologics, global technical operations at MSD Merck, says: "Although biopharma as an industry has lagged behind industries such as aerospace and electronics, we are learning from others and taking initial steps.

"The need to better connect information technology and operational technology systems, which may be different at various facilities, is a challenge. Another hurdle to be overcome is developing the capabilities of the workforce to use new tools and systems."

Adopting Pharma 4.0 involves a commitment and adequate resource allocation by the IT department to ensure necessary connections are made and maintained.

Although modern information and communication technologies, such as big data analytics and cloud computing, will help early detection of defects and production failures, as more databases connect with the cloud, security issues are commonly cited as a barrier to embracing the new tech.

Pharma 4.0 is not just about improving the outlook for big pharma, it is also about delivering better care to patients.

A case in point is Brainomix, a UK startup that developed e-Stroke Suite to improve the performance of brain scan interpretation for stroke patients. The technology is now being used in hospitals across the UK. Using artificial intelligence (AI), it makes data-rich image sharing between hospital departments easier, supporting healthcare professionals to make faster, more consistent and more informed decisions about treatment, and to identify patients who need to be transferred to specialist hospitals.

The development of this technology was possible after Boehringer Ingelheim, the German pharma giant, invested in Brainomix as part of its own commitment to Pharma 4.0. Boehringer Ingelheim is transforming its research, clinical development and production facilities to take full advantage of digitalisation

Pharma 4.0 is on a trajectory of inexorable growth. Transformation is moving so quickly it is almost impossible to predict what the technological landscape will look like more than just a few years into the future. The pharma industry has to respond now, rather than wait for an unachievable perfect jumping-on point. Collaboration with startups and other catalysts of innovation is playing an increasingly important role in driving positive digital transformation in health.

Industry 4.0 presents both opportunities and challenges for the pharmaceutical manufacturing industry and there is no one easy road to adoption. However, by implementing the correct standards and fully exploring the possibilities offered by emerging technologies such as AI, the industry can find a way to embed Pharma 4.0.

OPINION

‘The very factors that drive the success of the generic market in the UK may be under threat’

The success of the UK generic market is founded on high volume of use, low barriers to market entry and low levels of intervention. It is a tried-and-tested method which sees three quarters of all prescription medicines in England met by a generic product. Every year, generic medicines deliver more than £13 billion of savings to the NHS due to competition between manufacturers.

The market mechanics are so simple and effective that they are often overlooked. Large pharmaceutical companies are awarded patent protection on the successful products they develop and manufacture.

For every product that makes it through the strict regulatory process, there are many others that don’t get past the research stage. Therefore, to incentivise these companies, they are granted the exclusive rights to manufacture and market the medicine and thus sell it to the NHS. This period of exclusivity is typically in place for around 15 years.

Once that period of exclusivity is up, generic manufacturers market their own products, which have the same clinical outcome for the patient. This means the NHS is then able to choose from multiple suppliers of the same product, typically between three and ten companies at launch, and therefore the price decreases due to competition.

On average, the price of a medicine quickly reduces by about 90 per cent compared with its on-patent cost at launch. This saving means money can be invested elsewhere and more patients can be treated for less cost. Multiple suppliers also add to the security of supply.

It is a simple and successful formula that sees generic products fulfil around 75 per cent of all prescriptions in England for just under a third of the total cost the NHS spends on medicines, including £800 million funding for community pharmacy from generics.

However, as newer medicines evolve, this model may be challenged. The future pipeline of molecules coming off patent will focus on more targeted patient groups, increased innovation in terms of medicines delivery and more complex conditions.

The volume of use of these newer products will be lower, regulatory barriers to entry will be higher and there is a risk of greater government intervention in the market. The very factors that drive the success of the generic market in the UK may be under threat.

This will change the model for generic medicines manufacturers. For example, historically most products have been dispensed in primary care by pharmacy, with lower volume products being used in hospitals, at home and in clinics. With the advent of more complex medicines, this split may become more equal, which presents additional challenges.

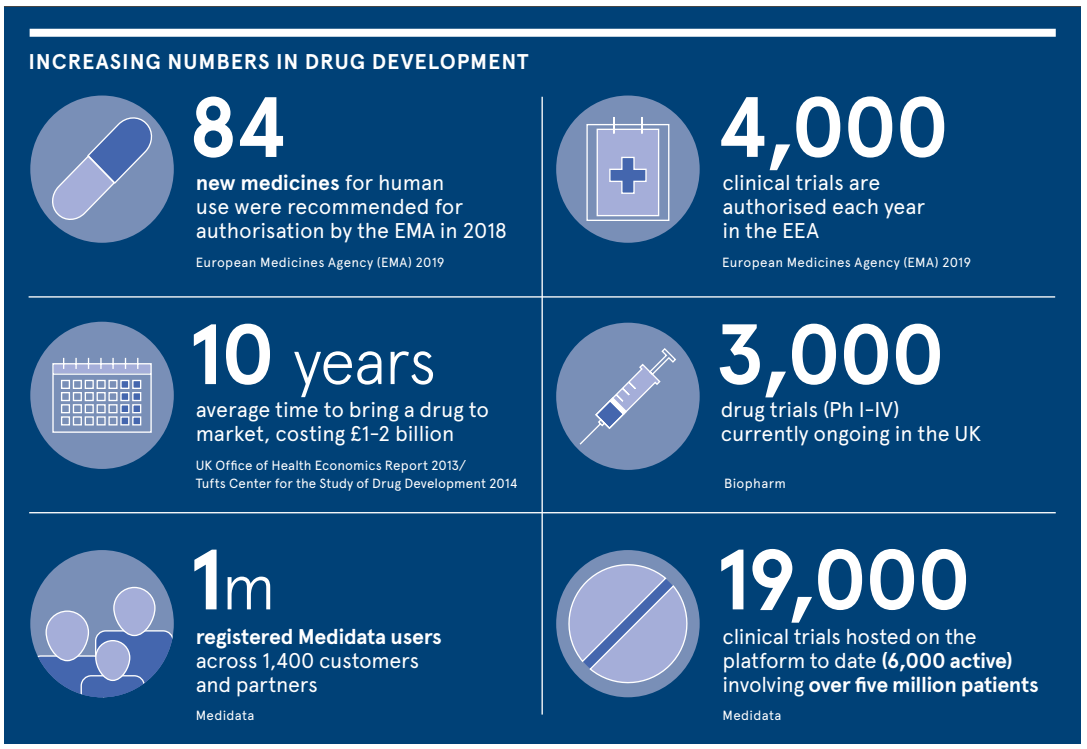
Often manufacturers will take a whole-market approach across their portfolio of medicines where some products are priced so they are profitable, while others will be supplied at cost or even at a loss. This holistic approach maintains supply for a large range of medicines, while allowing companies to make a profit on their overall investment.

With the market dynamics changing and for more complex medicines to become available and perhaps only used by a smaller number of more disparate patients, it is important manufacturers can balance their approach commercially.

Therefore, the traditional bedrock of high-volume, low-cost generics needs to be maintained in a way that allows companies to make the investments required for the development of more complex treatments. This could mean average prices, which are currently some of the lowest in Europe, potentially rise.

Allied to this is the inevitable transformation of the market in terms of delivery of medicines. The future would suggest an increasing need for digital pharmacy and home delivery. So, for a variety of reasons, a critical sector of the healthcare industry, which has thrived on a model of simplicity, will need to adapt to transformative change, while maintaining its mission-critical goal of ensuring the right medicine gets to the right patient at the right time. ●

Warwick Smith
Director general, British Generic Manufacturers Association



Drug development goes digital

Strategic use of patient data is signalling a bright future for drug development in the face of unprecedented global healthcare challenges

Rapidly ageing populations living with increased co-morbidities and stretched financial resources are placing huge strains on healthcare systems.

Traditional drug development is slow, unpredictable and cloaked with prohibitive costs, but the digitalisation of clinical trials, use of data and application of new technologies is now providing accelerated pathways to new treatments and energising scientific potential.

It takes an average of ten years and between £1-2 billion to get a drug to market. By collecting, analysing and harnessing clinical and patient data more efficiently, we can drastically reduce time and cost while also providing enhanced scope to find novel therapies.

“We are starting to see what is possible and there is a great future ahead,” says Christian Hebenstreit, senior vice president and general manager of Medidata, EMEA.

Medidata, a Dassault Systèmes company, is the leading software provider for managing and running clinical trials and streamlining drug development. The company’s innovative platform has powered 19,000 trials involving more than five million patients.

“Our science and technology is generating a huge amount of data that is then translated into value in the quest to get the right drug to the right patient at the right time,” says Mr Hebenstreit.

“We are seeing tremendous progress in a number of therapeutic areas, especially as we are looking into rarer diseases and different areas of cancer. This is thanks to the power of data and the ability to digitalise the drug development process and manage a clinical trial from one streamlined platform, from trial design and patient recruitment to regulatory submission and approval.”

Recruiting suitable patients for clinical trials is a ponderous process and retaining them can be an issue that massively impacts the outcome. Digitalisation has helped to identify the right patients, made it easier for them to take part, and has also opened up a wider and more diverse patient population.

A promising 28 per cent of clinical trials can now be completely virtualised with data collected and interrogated to provide the key findings across efficacy and safety, while often revealing fresh areas of research and patient benefit.

“We work in a highly regulated environment for very good reasons as we are dealing with people’s lives and some testing will not change,” says Mr Hebenstreit. “But finding the right patients to fit the criteria of a trial is one of the biggest issues for companies. It is complicated and can take months to recruit, particularly as many patients might face geographical, cultural or financial barriers.

“Opening it up to home-monitoring for patients, who may live 200 miles away or even in a different country, is a game-changer. Patient recruitment, enrolment and retention is suddenly more efficient. We are also able to replicate control groups for clinicians using historical data, automate processes, remove duplicative data entry and spot errors immediately. It saves time, reduces costs and is ethically very positive as more patients can participate in the trials and therefore get access to new drugs and better treatments much sooner.”

Digitalisation is also acting as a research catalyst promoting collaboration across big pharma and networks of research institutions and startups that now have an open landscape to test novel ideas once restricted by silo mentalities and prohibitive project costs.

Regulatory authorities are fully behind digitalisation and we are seeing more collaboration between the public and private sectors within life sciences than ever before. Medidata regularly engages with regulators around the world with common goals of improving patient experiences and clinical trial outcomes.

The German government, for example, has recently taken it a stage further by including digitalisation in clinical trials in new legislation designed to advance drug development and improve healthcare.

“The industry continues to push for more innovative solutions and the use of data science, big data and new technologies. And the encouragement from regulators is strong because they can see the opportunities coming from digitalisation,” says Mr Hebenstreit. “It benefits providers, physicians, hospitals, pharmaceutical and biotech companies and, most importantly, will help us to improve the lives of patients.

“Europe, and especially the UK, is well placed to make the best of digitalisation, especially as we explore the phenomenal potential from new technology, artificial intelligence and machine-learning. The change is already here. There is a lot of work to be done, but the future is exciting.”

For more information please visit www.medidata.com

medidata joins DASSAULT SYSTEMES

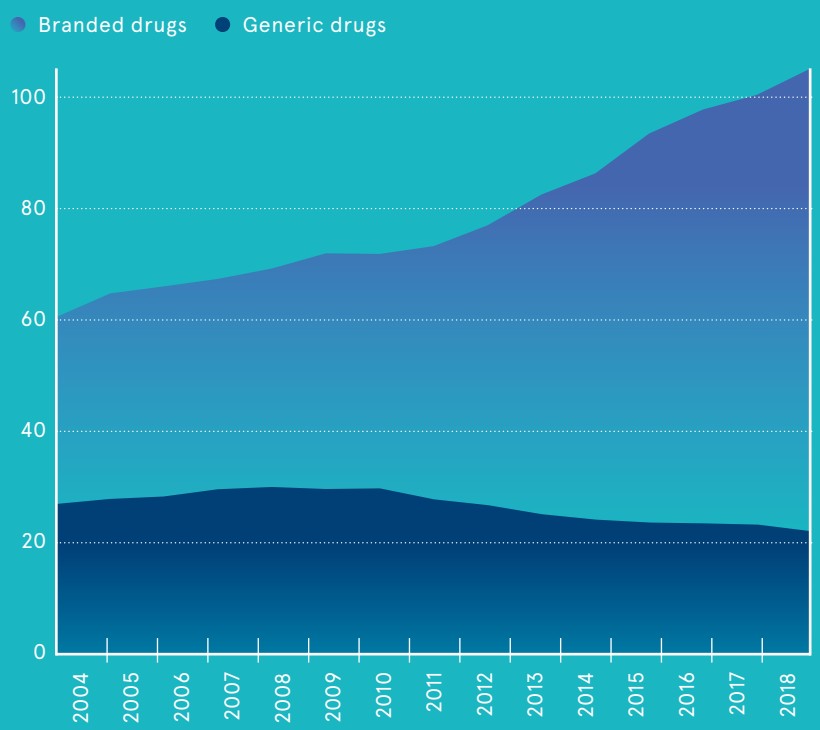
THE GLOBAL RISE OF GENERICS

In many countries around the world, scepticism around generic drugs endures, in spite of the fact that they are "bioequivalent" to (chemically the same as) their branded counterparts. But this attitude seems to be shifting as much cheaper generic drugs make up an increasing share of the global market, receiving a larger proportion of drug spend and, in so doing, saving countries billions of dollars

AVERAGE RETAIL PRICE FOR GENERIC AND BRAND NAME PRESCRIPTION MEDICINES

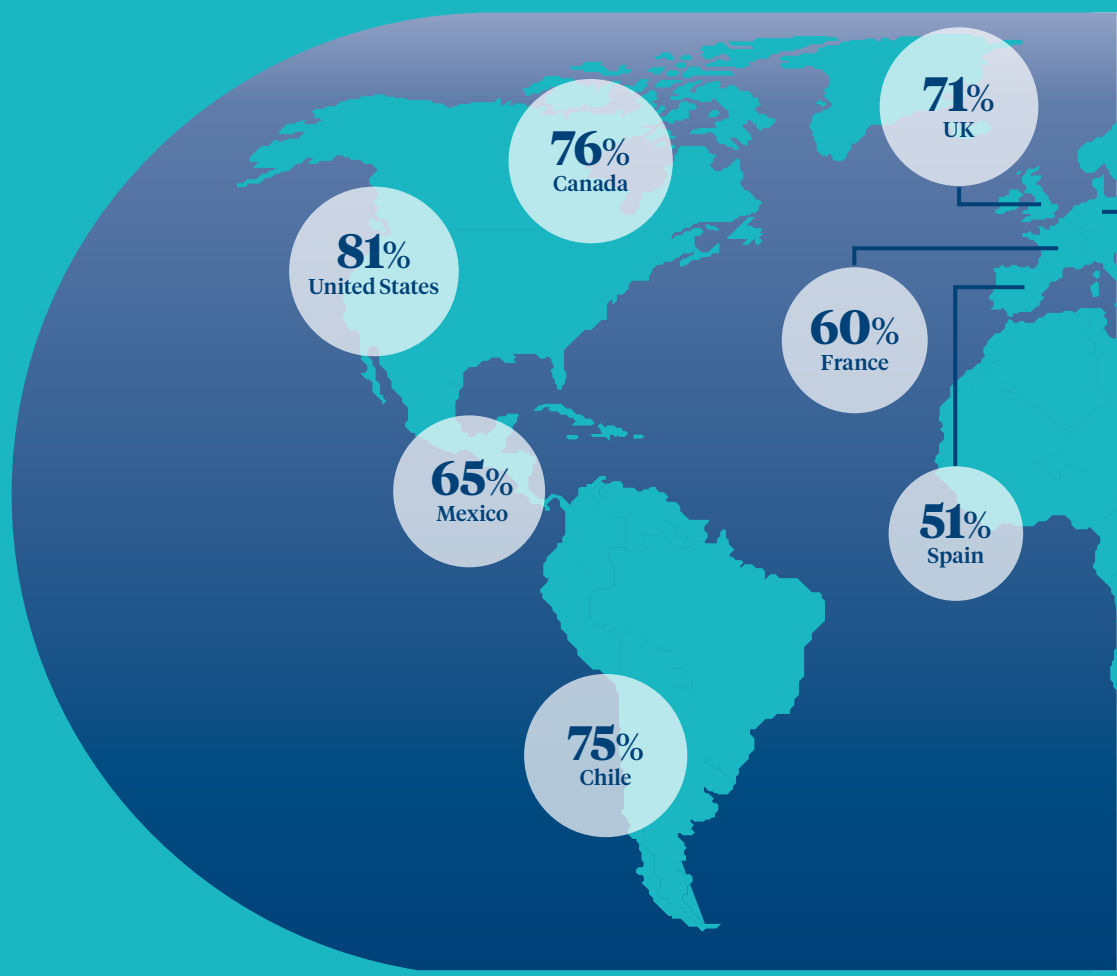
Canadian market (**Canadian dollars**)

QVIA and Canadian Generic Pharmaceutical Association 2019



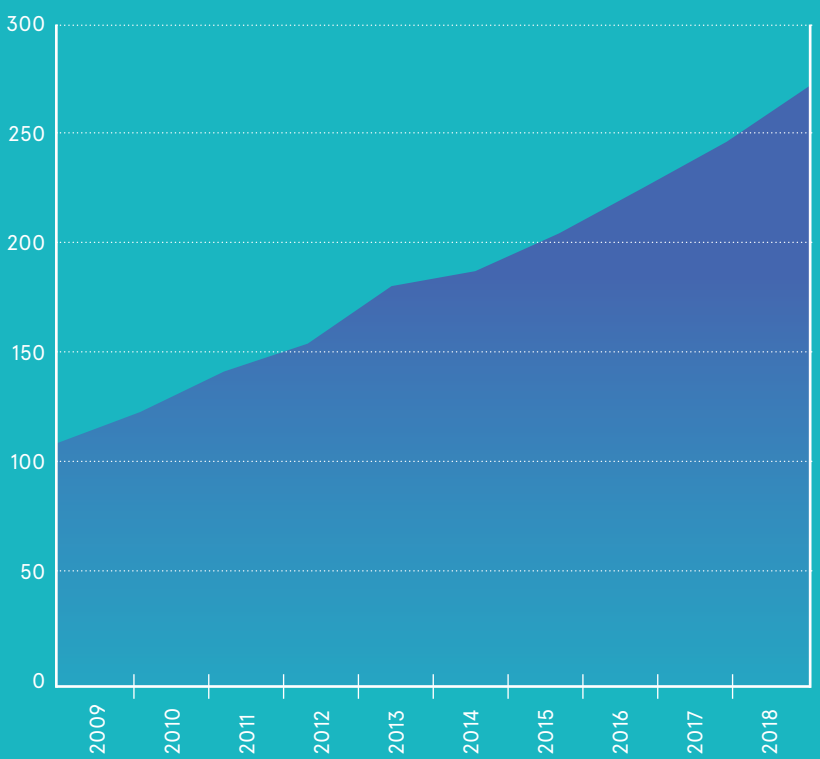
PERCENTAGE OF ALL PRESCRIPTION DRUGS SOLD ATTRIBUTABLE TO GENERICS

By selected OECD countries in 2018



ANNUAL SAVINGS FROM GENERICS IN THE UNITED STATES ($BN)

Association for Accessible Medicines 2019



PROJECTED GENERIC PHARMACEUTICALS MARKET VALUE IN LATIN AMERICA

Projected value ($bn)

Statista 2019

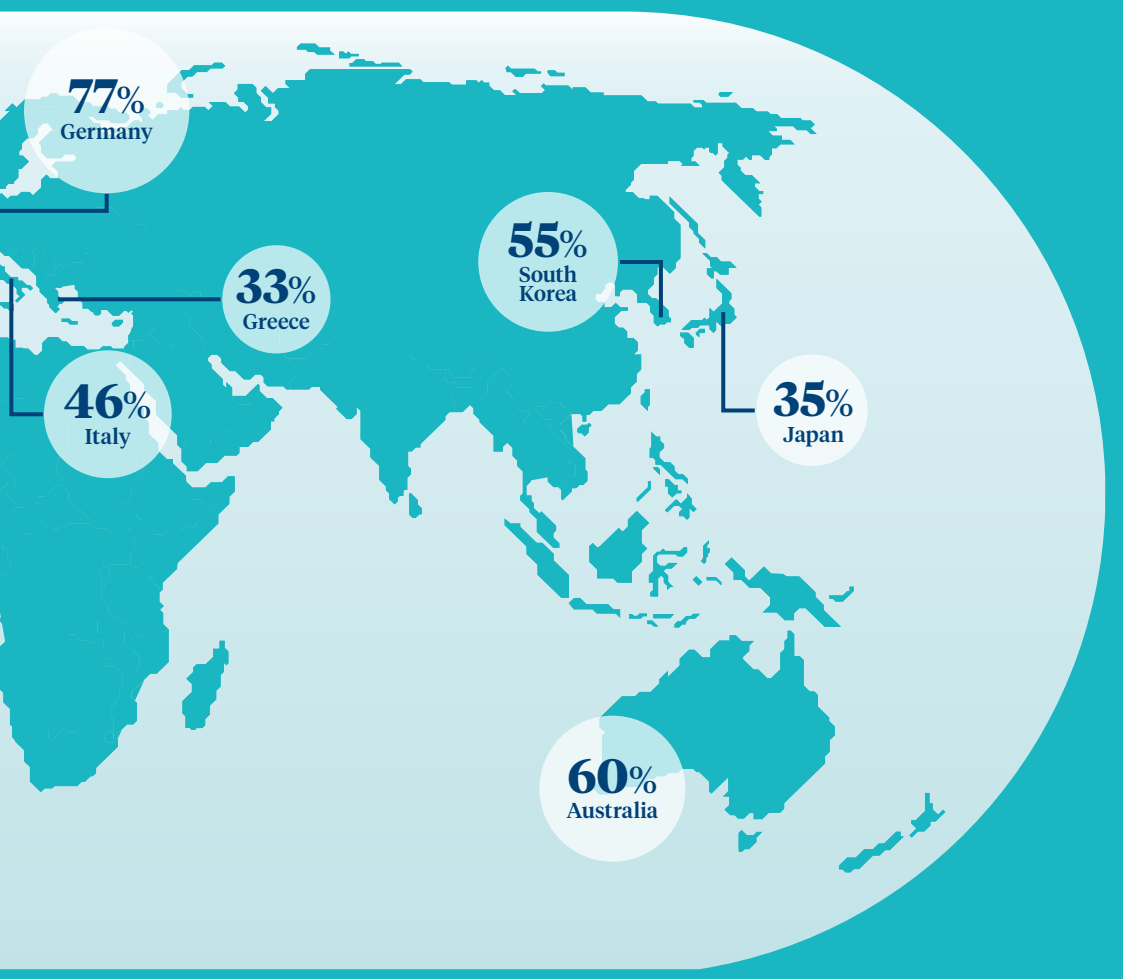
WHAT GENERIC DRUGS HAVE DONE FOR THE UNITED STATES

$2trn
saved by the healthcare system over the last ten years

$5.7bn
saved per state in 2018 alone

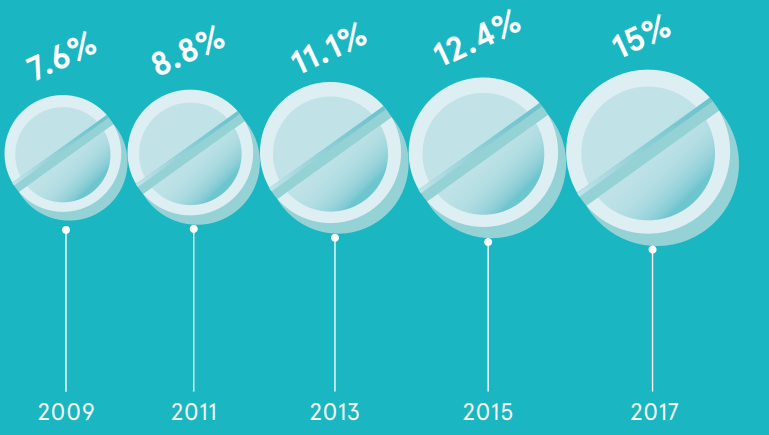
But only
22%
of drug spending has gone towards them

IQVIA 2019



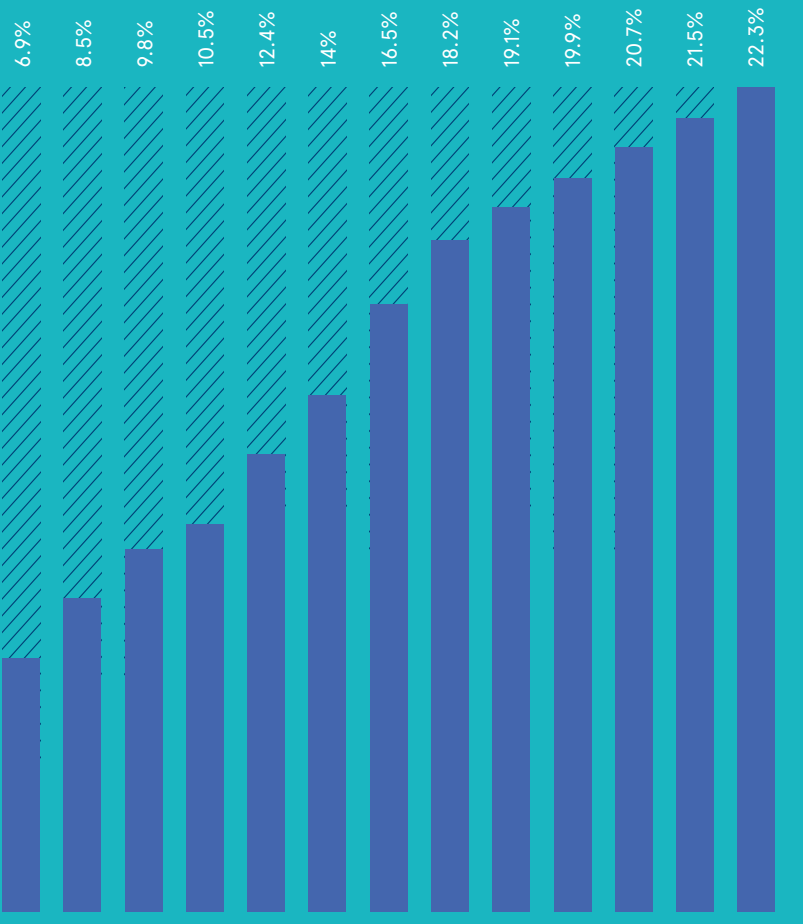
SALES SHARE OF GENERICS IN THE JAPANESE DRUG MARKET

Ministry of Health, Labour and Welfare 2019



VOLUME MARKET SHARE OF GENERIC DRUGS IN ITALY

Assogenerici 2018



PROPORTION OF MEDICINE SPEND ON GENERICS VERSUS BRANDS

UK spending (£bn)

National Audit Office with Department of Health & Social Care 2018

Commercial feature

Big data can help rescue healthcare

Innovative use of transformative big data can bring medicines to those in need, improve healthcare systems and empower patients

The big data era is upon us and with it comes the potential to unlock new levels of science to tackle global healthcare's mounting challenges.

This treasure trove of information and insights is the connective tissue of medical intelligence and has the power to drive new drug discoveries and influence health behaviour for the good.

It also represents the most potent weapon society has in the face of an ageing population struggling with multiple co-morbidities. The World Health Organization warns that all nations face challenges to cope with a demographic shift and, for the NHS in England and Wales, that means dealing with an extra 1.2 million people aged over 85 by 2033, representing an 80 per cent increase.

The salvation comes from understanding and deploying the reservoir of data generated from everyday health touch points, clinical trials, academic research and drug development data, says Gaetan Leblay, UK and Ireland managing director of Janssen, the pharmaceutical companies of Johnson & Johnson.

Janssen is beginning to power ahead with the innovative use of transformative big data to bring medicines to those in need, improve healthcare systems and empower patients.

"Access to big data could completely change how medicines are developed in the future," says Mr Leblay. "A tremendous amount of data is generated every day and all of us now have a wealth of information at our fingertips. The key part is how we connect the dots to generate really impactful insights which can have a positive effect on society.

"Technology is advancing rapidly and giving us both better access to data and enhanced ability to use it. These are exciting times."

Big data, which ranges across a spectrum from a patient's response to a therapy to cutting-edge laboratory interactions, opens up new horizons for scientists and supports policymakers in structuring healthcare systems to meet current and future needs.

Its potential is accelerated by an open and progressive approach which Janssen embraces. It is a key member of two groundbreaking collaborations that are developing machine-learning and algorithms to supercharge pharmaceutical industry data.

The three-year MELLODDY (Machine Learning Ledger Orchestration for Drug Discovery) project, which has investments of €18.4 billion, aims to increase efficiencies in drug discovery by training machine-learning models across datasets held by its 17 partners, including pharmaceutical companies, university research teams, startups and computing specialists.

It uses a platform for algorithms to trawl through the respective companies' data, without giving up any secrets, to invigorate drug development and punch a hole in the forbidding £1.9-billion and 13-years-to-market metric.

Gaetan Leblay
UK and Ireland managing director of Janssen

> **If we used data to intervene earlier, it is possible we may stop people from ever becoming sick in the first place**

The BD4BO (Big Data for Better Outcomes) research programme, launched in 2016, is accessing, harmonising and analysing data to focus on delivering advances in the treatment and management of Alzheimer's disease, cardiovascular diseases, prostate cancer and haematological malignancies.

Both projects chime with Janssen's DNA of transforming individual lives and the way diseases are managed, interpreted and prevented.

"I am very positive about the future because there is an opportunity to reinvent healthcare," says Mr Leblay. "At the moment, only around 10 per cent of healthcare budgets are dedicated to prevention with most of the remaining budget going on treatment.

"If we used data to intervene earlier, what we call at Janssen 'disease interception', it is possible we may stop people from ever becoming sick in the first place, while at the same time offsetting a lot of the costs because you are stopping diseases before they have the chance to take hold. This is a great prospect which is why we are pushing hard at it.

"Big data can also give us a better understanding about what is going on in the delivery of healthcare, at the system level, and through those insights you can start to create efficiencies."

The use of data can be an empowering educational tool for the public, giving them knowledge, underpinned by scientific research, which guides better health behaviour.

"Having insights at all levels – patient, prescriber and policymaker – is going to really help make a difference," says Mr Leblay.

Understanding patient behaviour – how a person responds to a diagnosis, a treatment plan and the medicine itself – is made easier by big data which enriches real world evidence alongside academic research and clinical trials.

"Together, this data can give us insights we just didn't have in the past. Insights that will allow us to increase the likelihood of treatment success and help healthcare systems to run more efficiently," he adds. "This in turn, could lead to more sustainable healthcare by stopping unnecessary treatments for example, or by making medical interventions at the optimal time.

"It can also give us a 360-degree view of a patient, enabling their progress to be followed, and helping healthcare professionals and their patients to make the best treatment decisions together.

"Ultimately, big data gives us fresh intelligence and a huge opportunity to improve the lives of patients and their families."

Janssen is putting its big data ideas into action across the UK and last year signed a five-year joint-working declaration with the Welsh government, Public Health Wales, and Cardiff and Vale University Health Board to develop a personalised database to analyse the outcomes for patients with myeloma.

It is also a mainline supporter of the world-leading project to complete the genome sequencing of all 500,000 UK Biobank participants, in collaboration with the government's UK Research and Innovation agency. The data it generates will sharpen understanding and shape treatments and prevention of diseases such as cancer and dementia.

"We have the potential to positively impact global and individual health with big data," says Mr Leblay. "Our goal is to be at the forefront of innovation, embracing the most advanced technologies and contributing to game-changing initiatives. But we cannot solve this alone, everyone has a piece of the puzzle and we have to work together.

"With a wealth of scientific heritage, I believe Janssen is well placed to play a key role in connecting data insights and helping to shift the healthcare paradigm, not just on the treatment side, but in prevention and disease interception too.

"Our vision of creating a world without disease is what we work towards every day and I am certain big data will be vital in helping us to achieve this."

For more information please visit janssen.com/uk

janssen | Pharmaceutical companies of Johnson & Johnson


Hero Images/Getty Images

AGEING

We need to redefine and rethink ageing

Could reclassifying 'ageing' as a disease or condition alleviate the suffering that accompanies getting older?

Marina Gerner

We all age as time goes by. The idea that ageing is a natural and inevitable process is ancient. So much so, that when a nonagenarian dies, we say it's "of old age" or "natural causes". Even though the actual causes are age-related diseases. Now, some scientists argue that we need to redefine ageing.

David Sinclair, geneticist at Harvard Medical School, says ageing should no longer be seen as a natural consequence of getting older, but as a condition in and of itself. What could be the implications of a new definition? The World Health Organization and the US Food and Drug Administration classify diseases and this guides how drugs can be trialled, prescribed and sold. It could also direct more research and investment into the field.

Could changing the way we conceptualise ageing therefore revolutionise healthcare? And if so, would the pharma industry start producing compounds to tackle ageing?

But first, how to define ageing? There is a range of views on this. "Based on science, ageing can be seen as a function of molecular mechanisms and diseases in addition to hereditary genetic factors and epigenetic factors, responding to lifestyle, nutrition and our natural and social environment," says Alexander G. Haslberger, professor at the University of Vienna's nutritional department and board member at Verita Healthcare Group.

When biologists talk about ageing, they refer to the deteriorative part of the process as "senescence" to avoid confusion, says David Gems, professor of biogerontology at University College London. "Senescence is deteriorative change and it's clearly pathological."

Critics say that classifying ageing as a disease would further stigmatise older generations or that it might divert attention from encouraging healthier lifestyles.

Those who say, "'let's celebrate ageing, it's not a disease' miss the mark", argues Professor Gems. Such arguments are well intended, but overlook the "real urgency of trying to do everything possible to prevent all aspects of senescence, the main cause of disease in the world. To say that 'suffering in later life, that's OK' is inhumane", he says.

A fruitful line of analysis "is to recognise ageing is the main risk factor for a host of diseases that restrict and kill people in later life: coronary heart disease, stroke, type-2 diabetes and dementia", says Alan Walker, professor of social policy and social gerontology at the University of Sheffield.

"I'd call it a condition, not a disease," says Professor Warren C. Ladiges, of the University of Washington, who is director of the Geropathology Research Network. "It's multi-factorial; there are a number of mechanisms and processes that are involved, and they can't be targeted with one magic bullet."

Even if ageing is not redefined as a disease, many scientists agree that the way we address ageing needs to evolve. Why is that? The change in perspective is a fundamental shift in medicine, argues Luigi Ferrucci, scientific director of the National Institute on Ageing in the United States. If the biological mechanisms of ageing are fixed and unchangeable, then the study of ageing becomes a "speculative science", he says.

But if we acknowledge that ageing is at the root of most chronic diseases and, if the mechanisms of ageing may be modulated, then understanding ageing opens incredibly powerful perspectives, says Dr Ferrucci. He argues that slowing down ageing will affect all diseases and could truly expand people's health-spans. This, in turn, would curtail the cost of healthcare.

Over the last few decades, scientists have gained new insights on how different organs age and how people have different levels of resilience in the face of ageing. Studies in mice, for example, have shown what happens when cells age and scientists have effectively used drugs to extend the lifespans of mice.

Research has revealed that so-called longevity genes, which control our health and fitness, can benefit from exercise and intermittent fasting. Alternatively, they can be boosted with drugs, as the experiments with mice have shown.

Some of the drugs that extend lifespans, and protect from a number of age-related diseases, are already in use for specific diseases, rather than overall ageing. Metformin, for example, is a common drug for type-2 diabetes. In the TAME (Targeted Ageing with Metformin) study, run by the American Federation of Ageing Research, healthy men and women in their early-60s were asked to take the drug. The study had a small sample, but its results were positive.

This study illustrates that "the pharmaceutical industry has started to produce compounds for the improvement of ageing-relevant mechanisms and diseases", says Professor Haslberger. "However, they need a new molecular understanding of the ageing mechanism as fast as possible to take this to the next stage."

Would these developments be likely to spark more interest from the pharma industry? "If drugs could be developed that might be taken regularly by humans for many years, say from middle age, to prevent age-related disease, then the pharma industry might be interested," says Professor Janet Lord, director of the University of Birmingham's Institute of Inflammation and Ageing.

Is a change of definition the first step to revolutionising the field? "Some scientists believe that if ageing is classified as a disease, then you could design and run clinical trials to slow ageing, as the regulatory bodies only approve trials and drugs for disease indications. Currently this is circumvented by carrying out trials to reduce features of ageing such as frailty or age-related diseases," says Professor Lord.

Given that current clinical trials tend to use repurposed drugs, "what may be much more effective and entice pharma to invest is to have new drugs designed specifically to target ageing", she says. "Pharma, in my opinion, is not likely to invest in this area and it needs investment from government to get this exciting new field going."

A new definition "would help a little, but is not the major hurdle", says Professor Lord, pointing out that drugs are not tested on people with several conditions, despite most older people being "multi-morbid".

This concern is echoed by Christina Victor, professor of gerontology and public health at Brunel University London. "Most people live with multiple conditions, and we're bad at managing and treating those," she says. People might have a psychologist for dementia and an endocrinologist for diabetes, but they are treated in silos. Instead, you need a workforce that can deal with multi-morbidity in an integrated way, says Professor Victor.

Professor Ladiges is pioneering research on drug cocktails, which aim to address multiple age-related issues. "Many of the drugs we're interested in are already clinically approved," he says. "The question is, how do they interact when you take them simultaneously? It's just a matter of time until we bring the drug-cocktail concept from the laboratory to the clinic."

> **There are a number of mechanisms and processes that are involved, and they can't be targeted with one magic bullet**

23%

of people aged 50 to 64 have three or more long-term health conditions

36%

of men over 80 need help with the activities of daily life (such as washing and dressing)

49%

of women over 80 need help with the activities of daily life

Centre for Ageing Better 2019

INDIA

India: a growing pharma powerhouse

India's economy may be struggling, but its pharmaceutical industry is booming, thanks to initiatives to improve domestic access to medicine and a solid export market. But can such growth continue?


elkor/Getty Images

Nick Easen

Despite the gloomy economic news coming out of India, the pharmaceutical sector still looks solid. Drill down and you realise why: the country is the largest provider of generic drugs globally and accounts for 60 per cent of all vaccines produced worldwide. It is a heavyweight in industry circles and the planet's third-largest producer of drugs by volume. These are astounding numbers.

While the country's economic growth sinks under 5 per cent, India's pharmaceutical industry is growing by 7 to 8 per cent a year, according to the Indian Pharmaceutical Alliance, while rating agency ICRA expects growth of 11 to 13 per cent in 2020. Strong demand is buoyed by better access to medicines in the domestic market, increasing spending on healthcare, and a higher incidence of chronic diseases.

"This is supported by a rising middle class whose disposable income keeps growing rapidly; a large proportion of these funds is being spent on healthcare and health insurance as the country and its people develop and mature," explains Vikas Bhadoria, senior partner at McKinsey & Company.

"Currently, Indian consumers are spending nearly 1 per cent of their total income on drugs and pharmaceuticals. With the rise in the per capita income, current spending is going to triple, to approximately $33 per annum, by 2020."

The market is already worth $38 billion a year, which includes exports. It employs 2.7 million people directly or indirectly and has world-class capabilities in formulation development. There's a strong entrepreneurial spirit with an established footprint in large international markets such as the United States. The industry is now India's fourth largest exporter of goods.

"The country's growing capabilities in contract manufacturing, research and development, as well as clinical trials, also make it a preferred partner for the global pharmaceutical industry," says Sujay Shetty, health industries leader for India and partner at PwC.

Then there's the *Ayushman Bharat Yojana*, launched only last year. This government healthcare programme is the biggest in the world and is aimed at providing affordable treatment for 500 million people, or 40 per cent of India's population, including 100 million vulnerable families.

"This is seen as an opportunity by pharma companies to help the underserved masses with affordable drugs," notes Tim Hoctor, vice president of professional services at Elsevier.

Still there are many challenges. Healthcare infrastructure in India is inadequate when compared to the size of its population. Roughly 29 skilled health workers are available for every 10,000 people in India compared with 41 in China and 111 in the United States. Fewer than a third of Indians have health insurance, the rest deal with medical bills directly.

"The inability to pay for medicines is another challenge that many people face. The Indian government's expenditure on healthcare is low, about 1 per cent of GDP compared to 2.5 to 3 per cent of GDP when analysing other developing economies such as China, Malaysia and Thailand," says McKinsey's Mr Bhadoria.

Despite the potential for growth in the Indian pharmaceutical industry, it is being squeezed from many sides. Generic drugs manufacturers are facing stringent pricing pressures from the government that is keen to make treatment more affordable, yet Indian medicines are already the lowest priced in the world. At the same time, growth in its key US export market is moderating, due to price erosion and greater scrutiny from regulators.

"Generics exports, specifically to the United States, have been a key driver of double-digit growth for top Indian pharmaceutical companies over the last few years. America accounts for over a third of total exports. Indian drugs reduce healthcare spend in the United States to the tune of over $20 billion every year," says Mr Bhadoria.

"Despite investments by some companies in newer product classes, such as biosimilars and specialty drugs, the contribution of non-generic products to the current revenue of pharma companies is miniscule."

> **Currently, Indian consumers are spending nearly 1 per cent of their total income on drugs and pharmaceuticals**

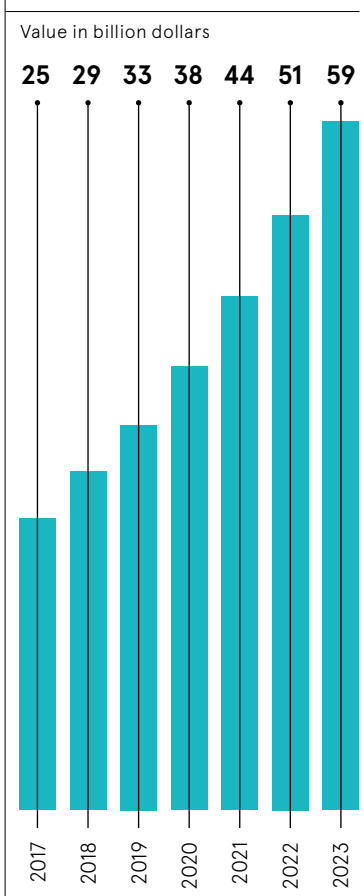
India's pharmaceutical industry has been slow to innovate when it comes to new molecules or complex generic drugs. There's also a limited government-supported research ecosystem. Certainly, there is scope to improve collaboration between state-run institutes and industry.

"A talent pool with advanced skills is also limited in India, with only 2,000 PhD students enrolled in pharmacy institutes, compared to over 15,000 PhD students enrolled in the United States," Mr Bhadoria explains.

As the disease burden in India transitions towards chronic diseases, there is rising demand for specialised medicines, which are currently more expensive than acute drugs. What India's pharmaceutical industry is extremely good at though is producing quality medicines at keen prices, especially when they fall off the so-called patent cliff. Therein lie future opportunities.

"India today is the primary supplier of essential medications for numerous disease areas worldwide, helping save millions of lives every year. If it extends this noteworthy cause of affordable, accessible medicine to the world, it could be a winner," Mr Bhadoria concludes.

VALUE OF THE INDIAN RETAIL PHARMACEUTICAL MARKET



India Brand Equity Foundation 2019

OPINION

‘It must become our goal that all countries and their citizens, not just the wealthiest, can benefit from breakthroughs’

Throughout the 2010s, advances in digitalisation have impacted every area of society, business and how we interact with the world around us. We have seen huge leaps in areas from artificial intelligence and deep-learning, to genomic sequencing and genetic engineering, which have already started to change the lives and expectations of patients.

As we look ahead to a new decade, sustained innovation in medical science, made possible by technology, will empower society to progress from a one-size-fits-all approach to one which is personalised, preventive and predictive, and dare we suggest, curative.

Hopefully, if I write a similar column in 2030, I’ll be looking back at a decade where 3D printing of organs became normal, regenerative and stem-cell medicine became widely accessible, and quantum computing-enabled research and development had started to show we could eradicate previously incurable diseases or improve their treatment.

Clearly, there is great promise in the future of pharmaceuticals around digital, devices, diagnostics and broader biologically based therapies, but there are also great challenges that will only be met by working together.

Changing global socio-economic and political factors will impact how the industry operates, and we must retain the ability to exchange ideas across borders to continue collaborating. Furthermore, trust is vital and citizen trust will be crucial to the future of pharmaceutical innovation, because without it data-sharing and availability will be severely constrained.

Equally, the industry must work to enshrine diversity as a founding principle at every level, from the make-up of clinical trial participants, to scientists at the bench, to caregivers and practitioners, to the boardroom. It must become our goal that all countries and their citizens, not just the wealthiest, can benefit from breakthroughs.

We will also find ourselves dealing with more ethical issues during the next ten years. Whether genome editing, highlighted by the interest in CRISPR-Cas9, or memory manipulation in the field of neuroscience to treat post-traumatic stress disorder, grappling with the implications of these questions will require a plurality of input from regulators, governments, academia, and pharmaceutical and healthcare organisations.

There are also likely to be emerging commercial challenges to the industry. New developments will come at a cost, and the entire ecosystem will need to agree on new ways to value, calculate and fund the costs of healthcare delivery.

Key stakeholders must evolve to become an integrated community embracing all aspects of healthcare, which will require deeply collaborative working relationships. It’s also not unlikely, given the effect of digitalisation, that we’ll see some of today’s technology giants competing and perhaps replacing some of the traditional research-based pharmaceutical companies.

Finally, the current skills shortage will become even more acute if we don’t come together to tackle it. The skills needed by the pharmaceutical and healthcare industry will need to evolve constantly due to the impact of digitalisation. Success will require an acceptance that the rate of change of the technology-science continuum is so rapid that extra effort will have to be expended to keep the workforce’s capabilities up to date, as well as a greater sharing of skills and best practices.

Through global co-operation and collaboration, I am confident we will have a chance to see these challenges can be met, and that we can continue to make significant strides in improving the health and wellbeing of patients around the world. This is an exciting time to be with a pharmaceutical company and I predict we will see significant changes in a few short years from now. ●

Dr Steve Arlington
President
Pistoia Alliance

Q&A

Connecting the dots along the pharma value chain

Industry leaders hold the “magic wand” to empower their talent to supercharge the potential of a patient-centric pharma value chain, says **Louis Hendriks**, founder and initiator of Global Value Web

Q What have you done lately?

A During my recent travels I’ve had the opportunity to exchange thoughts with senior healthcare and life sciences talent around the world. These talks underscore the challenge of identifying and connecting data to empower science and business. The itinerary hit key industry groups and events starting with #OHDSI in Bethesda, Washington, and then taking in travels across India with the Dutch Mission for Health, checking in at the excellent Pistoia Alliance meeting in Boston and on to the Globalize, Modernize and Transform at the ISPE annual meeting in Las Vegas, circled back via Bethesda for a “feet on the table” discussion with drug authorities, and finishing off in the UK with the Lab of the Future in Cambridge. The topics ranged across collaboration between healthcare and life sciences, the granularity of drug substances data and how the patient-driven value chain philosophy can tie it all together. Diverse topics, great conversations and one common denominator: data. Unfortunately, the data is loosely connected or not even connected at all.

All those great scientific minds, that passion to make healthcare better, still we are missing out on the full potential.

> “It’s industry leaders that can empower the industry scientists to become co-creators towards a patient centric pharma value chain

Q What can we do about it?

A Health and life sciences industry can collaborate so much better and put all that data into a logical context of bringing a quality product to the right patient, on time and in the right place. Thus, connecting the dots along the patient-centric pharma value chain. Let’s look at how a molecule transforms into a drug product and how it reaches a patient. Data, particularly connected data, empowers every aspect of that journey and brings value daily. Global Value Web executes on transformational data services that contribute, at the core, to the value chain transformation. We have proved through a variety of services that these steps transform disconnected data into a better functioning and more productive state. This in function of drug product reaching patient. There’s no lack of technology nor data. There’s lack of context. Value chain context.

Q And what are some observations here?

A One aspect is “control by data” and the drive towards a lean pharmaceutical-life sciences value chain. Increasing efficiency and effectiveness with focus on improved outcomes for patients, I believe, go hand in hand. Through my discussions, I realise so much more evangelist work is needed. There is a danger we remain stuck in a certain regulatory framework, and overall mindset, which some believe to be the only truth and that others are already bending towards the future. Another aspect is being trapped into a “data integrity” discussion, where data-integrity becomes the objective, rather than an outcome of an excellent orchestrated end-to-end patient value chain.

Q What’s the key takeaway from all this?

A The industry is at the cusp of massive transformational change which requires us to bring way more drug product to a far more variable patient base. Faster. Thus, causing an explosion of data. It all becomes visible in the industry’s global value chain and the transformation of it; towards globally integrated collaboration, directly driven by the need of the patient, enabled by data.

Q And where are we in the process of transformation?

A Making the switch from the old industries operating models to one single new health operating model may just be the transformational wave for the coming decade. We are now in the early days of that transformation.

Q Any closing thoughts?

A Yes, I’d like to call upon industry leaders to empower their scientific and business talent to increase their focus on their data; name it, own it, improve it! Scientists need to be able to take responsibility for their own content in a digitized environment. Content becomes data. Ask them to treat their data as pieces to a puzzle which represents a patient centric pharma value chain. Become co-creators.

My team and I are here to enable that. Working directly with the scientists and business process owners to get it in the right context. Driving true value.

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Global Value Web

ANTIBIOTICS

What are new antibiotics really worth?

Antimicrobial resistance is one of the greatest challenges of our time, but few new antibiotics are currently in development. The NHS is testing the world's first subscription-style payment model in an attempt to change this

Natalie Healey

Bacteria are better than any of us at adaptation. Reproducing in minutes, evolution can happen rapidly. This is how antimicrobial resistance occurs: the germ that develops armour to medication is able to pass this trait to its offspring.

It's survival of the fittest. Humans are constantly playing catch-up and need new antibiotics for when the older drugs no longer work. But we're simply not developing them fast enough.

Antimicrobial resistance is a huge and ever-growing problem. Resistant bacteria already cause more than 700,000 deaths globally every year. Former UK chief medical officer Professor Dame Sally Davies recently called for an Extinction Rebellion-style campaign to help people and politicians see that antimicrobial resistance is as much of a crisis as climate change.

Economist Lord Jim O'Neill agrees that public awareness of this issue is dangerously low. From 2014 to 2016, he led an international assessment, the Review on Antimicrobial Resistance (AMR), to analyse the global problem of rising drug resistance and propose concrete actions for tackling it.

"Antimicrobial resistance doesn't have its Greta Thunberg. But the consequences of not solving the problem are more known than climate change," he says. "It's a major dilemma. A lot of people think at the first signs of feeling slightly ill, go to the doctor and get an antibiotic. We need to stop treating these things like sweets."

> **A lot of people think at the first signs of feeling slightly ill, go to the doctor and get an antibiotic. We need to stop treating these things like sweets**

Greater awareness from the public could help as overuse of these medicines has led to the problem in the first place. But until pharmaceutical companies invest in new antimicrobials, the threat of a post-antibiotic era, when a simple ear infection could be fatal, will not go away.

Significantly, in July 2019, the Department of Health and Social Care announced that the NHS will test the world's first subscription-style payment model to incentivise pharmaceutical organisations to develop new drugs for resistant infections.

The trial will be led by the National Institute for Health and Care Excellence (NICE), NHS England and NHS Improvement. Pharma companies will be paid upfront for access to medication based on its usefulness, rather than the amount that will be prescribed.

We're used to paying for an antivirus subscription to protect our technology, so could an antibacterial equivalent be what's needed to safeguard public health?

Dr Anna Maria Geretti, professor of virology and infectious diseases at the University of Liverpool's Institute of Infection and Global Health, points out that something needs to change. The emergence and spread of antimicrobial resistance has outpaced innovation.

"Resistance to antibiotics is a growing threat globally. There is increasing mortality, especially with certain types of infections for which there are very limited treatment options, such as gram-negative bacteria, that are recognised by the World Health Organization as 'priority pathogens' and a global threat," she says.

But for a pharmaceutical company, research and development costs for a new antibiotic are far and above the revenue generated once the drug reaches the market. As the medicine will target a high-risk infection, its use would have to be restricted so pathogens do not become resistant to it too.

"Appropriate usage, although an important healthcare objective, is in conflict with pharmaceutical companies' revenue objectives," says Beth Woods, senior research fellow at the Centre for Health Economics.

That's where this new payment model comes in. It's based on "delinkage", where a drug's profitability is isolated from its volume of sales. The scheme proposes that pharmaceutical companies will be paid upfront for access to new antibiotics based on how useful they are expected to be for patients and the NHS, rather than how often they will be used.

Ms Woods is part of the team at the Policy Research Unit in Economic Evaluation of Health and Care Interventions, which provides cost-effectiveness analysis to the Department of Health and Social Care. Her group will come up with a value-based payment for the new antibiotics submitted for the trial.

The first phase of the project will focus on developing an outline for the payment model and selecting two antibiotics to undergo the assessment, which is likely to conclude at the end of 2020.

"We will learn through this trial how effective it is in bringing innovation to patients in need. In the forthcoming months, we expect to see the first concrete proposals from pharmaceutical companies to NICE, NHS England and NHS Improvement," says Professor Geretti.

Understandably, some people might feel queasy about the taxpayer creating incentives for big pharma. But is it so crazy that it just might work?

"It's the only initiative that any government anywhere in the world has come up with since the AMR review. So let's give it a chance," says Lord O'Neill.

But even if the UK scheme does turn out to be an important step in tackling antimicrobial resistance, to address global market failure of new antibiotics, other healthcare systems all over the world will need to follow its lead.

Another dilemma is whether the value NICE and the NHS place on a new antibiotic will be something that is truly attractive to pharmaceutical companies, while remaining economical for the health service.

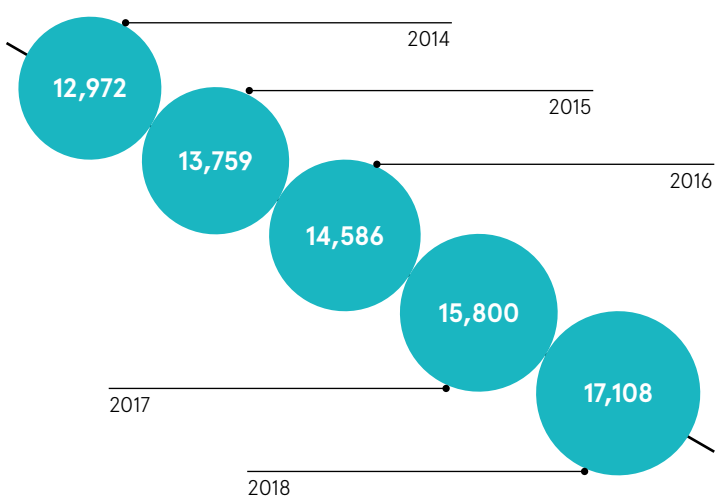
According to Rebecca Glover and colleagues from the Antimicrobial Resistance Centre at the London School of Hygiene and Tropical Medicine, the model could create "perverse incentives in the future, with companies holding back innovations in the hope that perceived value will increase as antimicrobial resistance rates get worse".

Lord O'Neill believes we won't see a significant shift on antimicrobial resistance until pharmaceutical companies show a firm commitment to putting public health before profit. "Less talk, more action," is needed, he says.

"The amount of talk about the role of pharmaceutical companies and new drugs that has gone on for the past four years is ridiculous relative to the action. I would like the pharmaceutical industry's leaders to show their Tesla moments," Lord O'Neill concludes.

RISE IN BLOODSTREAM INFECTIONS DUE TO ANTIBIOTIC-RESISTANT PATHOGENS IN ENGLAND

Number of resistant infections



English Surveillance Program for Antimicrobial Utilisation and Resistance (ESPAUR) 2018-2019

Commercial feature

Acino and Quay steer new course for contract development and manufacturing

As the era of blockbuster drugs comes to an end, pharma is moving towards drugs that are increasingly complex and made for small patient populations, creating opportunities and challenges for contract development and manufacturing organisations (CDMOs)

The CDMO industry started out decades ago as a niche service, offering additional manufacturing capacity or speciality services to pharmaceutical companies. Now pharmaceutical and biotechnology companies increasingly see CDMOs as an extension of their own development and manufacturing resources, providing capabilities that are fully integrated with their services and processes.

Many pharmaceutical companies are refocusing on their core capabilities and strengths, leading to divestments of in-house manufacturing capacities in some areas and to a growing reliance on CDMOs in others. Mid-size companies in particular are finding that partnerships can provide integrated manufacturing solutions in this new environment.

There is much at stake for pharmaceutical companies when choosing a partner for their manufacturing outsourcing needs. Proven reliability and impeccable quality standards are key to choosing a CDMO that must also be able to demonstrate the capability and experience to manage the technology transfer required to provide effective process solutions on an industrial scale.

The goal of technology transfer is to transfer product and process knowledge between development and commercial manufacturing and within or between manufacturing sites to achieve project realisation. This knowledge forms the basis for the manufacturing process, control strategy, process validation approach and ongoing continual improvement within the development phase.

Technology transfers are the most complex and time-consuming processes for a CDMO, especially because multiple partners and sites may be involved. However, successful partnerships between different teams can bring significant benefits to customers and, ultimately, to patients. Having a product developed while considering future scale and costs, and bringing together experts from all relevant functions, can make a positive difference.

> A new approach is needed, which will require a spirit of collaboration and integration

Felix Faupel, head of contract manufacturing at Acino, which offers a full service, best-in-class contract manufacturing for oral solid dosage forms, says partnering and flexibility are critical for mid-sized CDMOs in this fast-changing environment.

"When pharma companies or even startups begin their developments, it is crucial for the overall project calculation to understand how their products can be upscaled, commercialised and what their cost structure may look like in the future," he says. "The technology transfer to commercial scale is therefore a crucial step in every development journey and must be considered at an early stage. Integrated CDMO solutions can help to overcome this complexity because they evaluate a new development from end to end."

In October, Acino Contract Manufacturing announced a strategic partnership with UK-based Quay Pharma for the formulation and development of manufacturing processes for oral solid dosage forms.

Through the partnership, both companies will broaden their customer offerings and create a smooth and integrated path between pharmaceutical development provided by Quay and all commercial manufacturing services provided by Acino. Quay can offer clients access to Acino's extensive experience of commercial manufacturing of oral solid dosage forms, while Acino, based in Switzerland, is able to offer Quay's scientific excellence in pharmaceutical development to its contract manufacturing customers.

Maireadh Pedersen, chief executive of Quay Pharma, says: "Quay specialises in working with new chemical entities producing innovative and most effective formulations. This fits in perfectly with Acino's advanced capabilities in oral solid dose manufacture.

"Acino has a strong heritage in the provision of high-quality products and we look forward to working closely with Acino on being able to support our customers to successfully bring their new medicines to market."

The future of pharma depends on getting complex drugs to patients as quickly as possible. To make this happen a new approach is needed, which will require a spirit of collaboration and integration. This means working together to bring the drugs patients need through the different stages of clinical development to successful market registration. This is what we all want to achieve.

For more information please visit acino.swiss

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