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A new future for R&D?
Measuring the return from
pharmaceutical innovation 2017

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Contents

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Foreword

Welcome to *A new future for R&D?*, the eighth annual report from the Deloitte Centre for Health Solutions exploring the performance of the biopharmaceutical (biopharma) industry and its ability to generate returns through investment in innovative new products.

It has been a busy year, and we would like to thank everyone who provided feedback on last year's report through company presentations and industry level conversations. Based on these discussions, we believe the biopharma industry continues to face an incredibly challenging R&D environment and has yet to turn a corner in terms of its value proposition and returns. However, we have also seen some room for optimism, due to improvements in the efficiency of certain R&D processes and the wider adoption of new technologies. Many areas of unmet need also remain, although it has been a year where breakthrough drugs have made headlines, including the first FDA-approved chimeric antigen receptor T cell (CAR-T) therapies and the first digital pill.

These and other 'breakthrough' products represent potentially life-changing outcomes for patients and point towards a different economic model with faster development and approvals, and potentially lower development costs. The impact of these breakthrough drugs on industry returns will inevitably impact investment choices, and we look forward to tracking their influence on the development of products for larger populations with conditions where there have been limited treatments to date, including degenerative neurological conditions. Working on these areas of unmet need is likely to continue the current trend of increasing collaborations between industry and academia, which have the potential to improve returns for the industry.

This 2017 report provides estimates of the return on investment that 12 large cap biopharma companies might expect to achieve from their late-stage pipelines. Our analysis is focused on assets that are currently in late-stage development and expected to launch within the next one to four years, using data from publicly-available, audited, annual reports and forecasts provided by GlobalData.

For the third consecutive year, we track the performance of an extension cohort of four mid-to-large cap biopharma companies, which allows us to compare and contrast their performance against the original cohort. This helps deepen our insight into company and portfolio characteristics that produce higher R&D returns.

In our 2016 report, we focused on approaches that biopharma companies could employ to both positively influence the commercial success of their assets and drive greater R&D efficiency. This year, we have supplemented our core quantitative analysis with a view of emerging technologies that have the potential to optimise the research-based biopharma value chain.

We hope you find this report thought-provoking, and we welcome your feedback on the findings and the implications for the industry in the coming year.

Colin Terry
Partner, EMEA Life Sciences R&D Advisory
Deloitte LLP
colterry@deloitte.co.uk

Neil Lesser
Principal, US Life Sciences R&D Strategy
Deloitte Consulting LLP
nlesser@deloitte.com

Executive summary

Drug development continues to be challenging, complex, costly and time-consuming. This coincides with a growing tidal wave of confounding communicable and non-communicable diseases that threaten global public health. Although there are promising platforms emerging to tackle these complex diseases, the challenge will be to develop these platforms in an accelerated, efficient way to create near-term value for all stakeholders. It will require a transformed model that involves new paradigms for drug development and emerging technologies.

Since 2010, our series *Measuring the return from pharmaceutical innovation* has provided insight into the state of R&D in the biopharma industry. Specifically, we estimate the return on investment that 12 large cap biopharma companies might expect to achieve from their late-stage pipelines. For the third consecutive year, we also include an extension cohort of four mid-to-large cap biopharma companies in our analysis. The internal rate of return (IRR) that we calculate serves as a proxy to measure the industry's ability to balance investment (initial and ongoing capital outlay) with the cash inflows (drug sales) biopharma companies are projected to receive as a result of this investment. It also provides a basis for discussion and debate between payers, Health Technology Assessment groups and the biopharma industry, to help determine the value for money of innovation.

In analysing our results, we explore strategies used across the industry to maximise IRR, either by reducing the costs of R&D or by maximising the value of late-stage pipeline assets. This year, we also use a wider lens to look to the future, analysing some emerging technologies that we predict will influence the future of R&D dramatically. Overall, we aim to provide a view of R&D that helps biopharma companies overcome many of the challenges they face – and will continue to face – over the next several years as they strive to achieve a sustainable future, including bringing to market new medical innovations that demonstrate measurable value to patients.

Improving projected returns continues to be challenging

Over our series, we have seen projected returns for the original cohort of 12 large cap companies decline from just over ten per cent in 2010 to under four per cent for the past two years. Similarly, the extension cohort has seen its IRR decline from over 17 per cent in 2013 to just under 12 per cent this year, although this year showed an uptick of two per cent from 2016. These declines are driven by two factors:

- the increase in the average cost to bring an asset to market, to $1,992 million for the original cohort (from $1,188 million in 2010) and $2,173 million for the extension cohort (from $1,034 million in 2013)

- declining average peak sales, even though peak sales per asset increased between 2016 and 2017 for both of our cohorts, with the average peak sales per asset for the original cohort increasing from $394 million to $465 million and the extension cohort returning to blockbuster levels (from $801 million to $1,128 million).

While the extension cohort replenished their pipelines, the original cohort saw a sharp decrease in the number of late-stage pipeline assets in the last year, which had remained fairly consistent over the previous seven years. This decrease in asset numbers was the main driving force that led to the increase in the average cost to bring an asset to market for the original cohort. This suggests that the focus on developing assets that have higher potential peak sales is counterbalanced by a higher probability of failure. It is also possible that in the past year, the original cohort has purposefully removed a number of assets from their pipelines that they did not expect to meet regulatory or reimbursement thresholds for viability.

Overall, our analysis is a stark reminder that investing in biopharma R&D is risky, and financial returns are by no means guaranteed. Despite the decrease in returns for the original cohort, we see positives in the increase in forecast peak sales per asset, as companies target areas of unmet medical need and/or rare disorders. The ability of the original cohort to improve its projected returns from existing late-stage pipeline assets also represents an improvement from last year, showing the power of research that reflects real-world impact against either the standard of care or key competitors.

The search for innovation

The focus of this series has always been on projected financial returns and the outlook they provide for the future of biopharma R&D. However, it would be a mistake to use these projected financial returns as the only measure of the industry's ability to innovate. Despite many challenges, there are numerous examples of innovation that demonstrate biopharma's resilience and project optimism about the future – from the approval of numerous immunotherapies to the first ever approvals of chimeric antigen receptor T cell (CAR-T) therapies and first digital pill in 2017.

We have also seen an increase in the number of approvals of new molecular entities (NMEs), orphan, breakthrough or fast-track designations. This leads us to present an overall optimistic view of biopharma's potential, although in our view, much improvement is still needed across R&D to balance revenues and costs.

R&D process transformation through technology

In the coming years, the biopharma operating model will necessarily become leaner, as the future of work becomes a reality. This 'industrialisation' of biopharma will bring numerous transformational changes to how the industry functions, particularly in R&D. We see opportunities for biopharma to increase returns in the coming years if the industry embraces advanced technologies that can impact R&D across the entire value chain. Artificial intelligence, real-world evidence, and robotic and cognitive automation, to name a few, have the potential to improve study design, physician and patient recruitment and in-trial decision making, as well as increase efficiency and accuracy in repetitive tasks all the way through to regulatory filing. Similarly, social media, mHealth, wearables, connected devices, and telemedicine all have the potential to transform how patients are engaged in clinical trials, enabling expedited enrolment and improvements in study design and data quality, and increasing adherence and retention. Applying these technologies could lead to a vibrant and sustainable biopharma industry focused on high value outcomes – an objective that is vital to the future of global public health.

For the original large cap biopharma cohort:
Projected R&D returns continue to decline

10.1%	7.6%	7.3%	4.8%	5.5%	4.2%	3.7%	3.2%
2010	2011	2012	2013	2014	2015	2016	2017
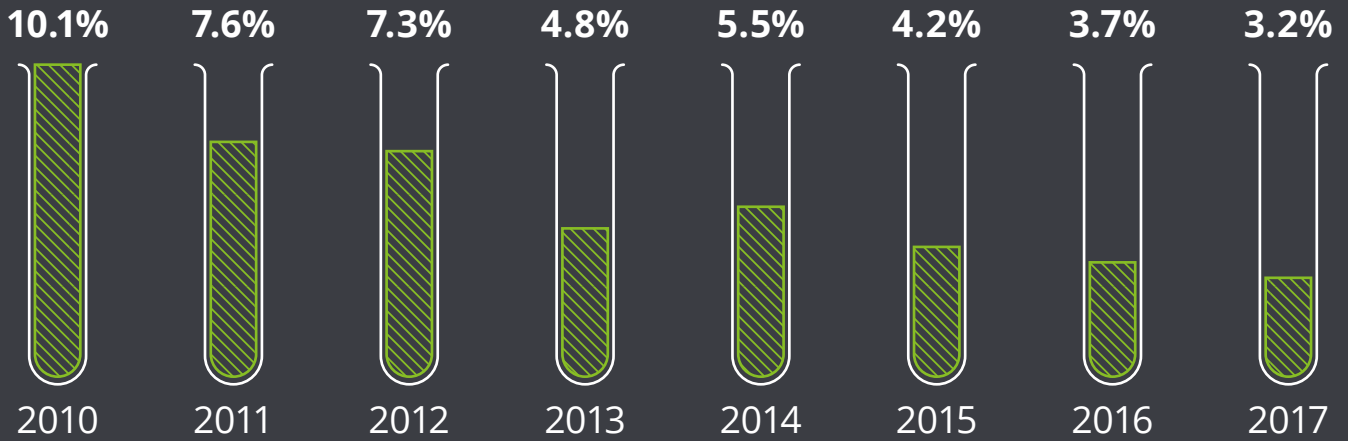
Cost to **bring an asset to market** has increased to record levels in 2017

2010
$1.188 billion

2016
$1.539 billion

2017
$1.992 billion

Projected peak sales per asset **more than halved** between 2010 and 2016 but have increased by 18% in 2017

2010
$816 million

2016
$394 million

2017
$465 million
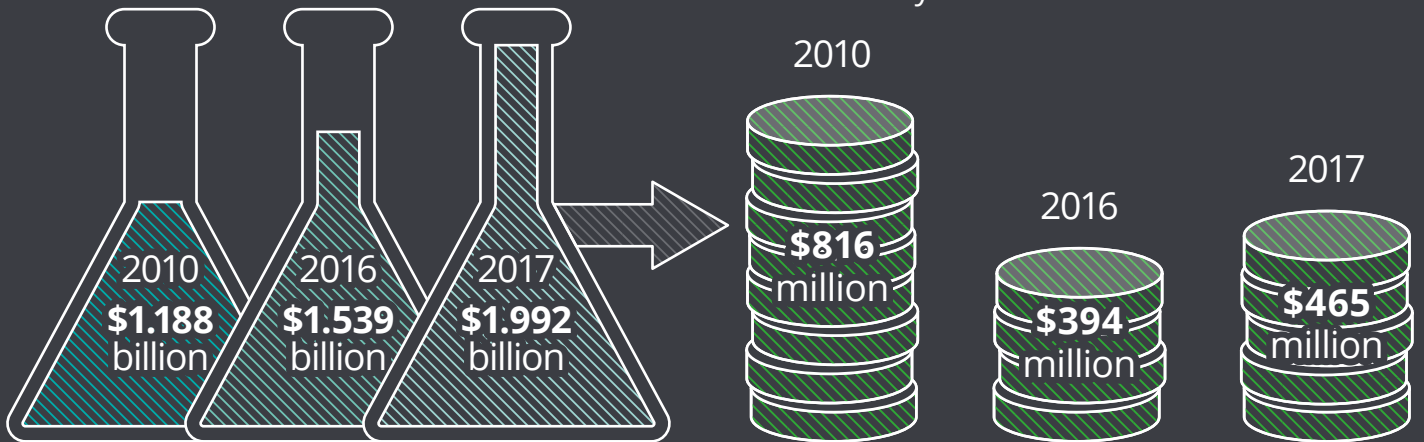
This year's uptick in cost per asset is driven by the decline in the **number of late-stage assets**, as fewer Phase III trials have started in the past year
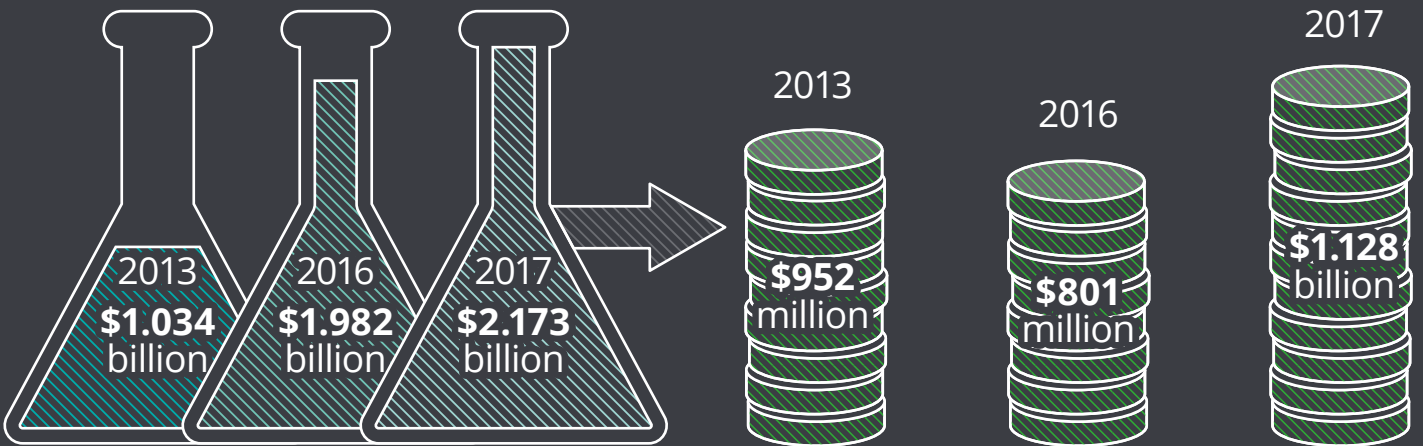
2016
189
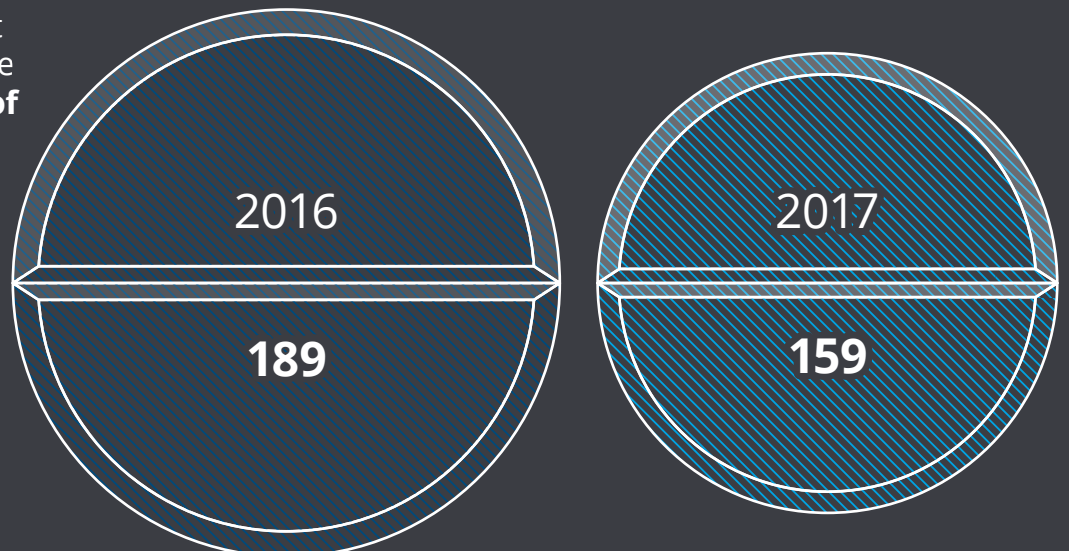
2017
159

For the extension cohort of mid-to-large cap biopharma companies:
Projected R&D returns are back up above **10%**

17.4%	17.7%	16.1%	9.9%	11.9%
2013	2014	2015	2016	2017
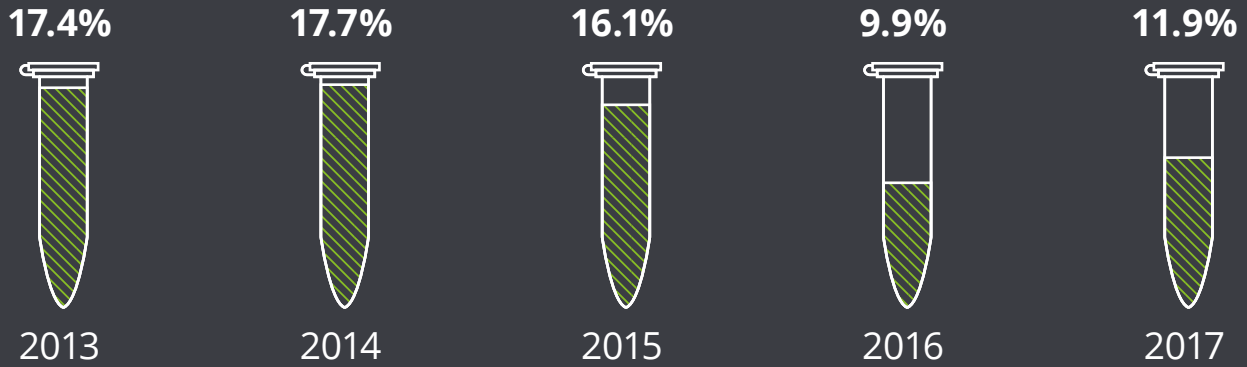
Cost to **bring an asset to market** has doubled since 2013

Projected peak sales per asset have increased to **blockbuster levels** in 2017

2013
$1.034 billion

2016
$1.982 billion

2017
$2.173 billion

2013
$952 million

2016
$801 million

2017
$1.128 billion

A digital remedy for R&D productivity

Artificial intelligence

Crowdsourced input into clinical trials

Real-world evidence

mHealth

Robotic and cognitive automation

Wearables and connected devices

Social media and online platforms

Telemedicine

The changing nature of R&D

Biopharma R&D is inherently a high-risk, high-reward endeavour. Every year billions of dollars are spent developing new drugs, and yet the vast majority of promising drug candidates never make it to market. The industry employs a cost recovery model to recoup investments in R&D, but with the overall cost of drug development remaining incredibly high, the industry faces a complex environment that makes recouping these costs increasingly difficult.

We have documented many of the challenges biopharma companies face in our series *Measuring the return from pharmaceutical innovation*, and we have analysed numerous strategies that the industry is undertaking to address them. Some of these challenges include increased competition and cycle times, shorter time in market, expiring patents, declining peak sales, pressure around reimbursement and mounting regulatory scrutiny. Very few, if any, of these challenges have been overcome at a company portfolio or industry level. Pricing remains perhaps the most publicised challenge, especially in the context of escalating overall health care costs, and payers are increasingly demanding that biopharma demonstrate the value of its products. It is no longer enough to show only product efficacy and safety at the point of registration; payers want to see improved outcomes, based on real-world evidence (RWE), as the foundation for a value-based pricing model.

Our 2016 report, *Balancing the R&D equation*, saw the lowest levels of projected returns since we began this series, as blockbuster costs were imbalanced by the lack of blockbuster revenues.[1] Following these results, we produced our first annual biopharma R&D leader survey, *Innovating to survive, collaborating to thrive*.[2] This report identified current priorities, future investment plans and key factors that are driving operational excellence in R&D, based on interviews with R&D leaders from across the industry, which we used to guide the development of this 2017 report.

With biopharma facing such difficult challenges, it is under increasing pressure to innovate. However, with the number of threats to global public health also increasing, biopharma has numerous opportunities to turn innovation into impact. We briefly examine some of the largest global public health threats, including a 'tidal wave' of complex age and behaviour related diseases that are now affecting countries of all income levels, along with the renewed threat of infectious disease. We also look at some of the successes biopharma has had recently in addressing these threats.

The tidal wave of complex diseases is growing

We explored the 'tidal wave' of age and behaviour related non-communicable diseases in our report *Facing the tidal wave: De-risking pharma and creating value for patients*.[3] These diseases, including cancer, dementia and diabetes, are expected to increase in incidence substantially in the foreseeable future and present numerous challenges to global public health. However, they also present opportunities for biopharma to be innovative and impactful in response to the tidal wave. Biopharma has already devoted significant resources to developing new treatments and has seen a number of successes.

While cancer remains the second leading cause of death globally,[4] immunotherapy has emerged as a transformational breakthrough in cancer therapy. Many immunotherapies have been effective in treating rare cancers and cancers that are resistant to chemotherapy and radiation treatment. This has offered hope that future innovation in cancer modalities will result in long-term remission rates across hundreds of types of cancer. However, this optimism has also been met with a new set of challenges. For example, the number of patients required to complete over 1,000 clinical trials that are currently underway using new immunotherapies has created a logjam; there are simply not enough eligible, accessible patients to complete every trial in the required timelines.[5] Additionally, while improved outcomes have been observed in some patients, many immunotherapy treatments are only efficacious for a select group of cancers and in a subpopulation of patients with those cancers. This variability is compounded by the difficulty of producing predictive models of treatment efficacy and patient response.[6] These and other challenges demonstrate that immunotherapy is still in its infancy, although it has a promising future.

Meanwhile, dementia patients and their carers have had little reason for optimism in recent years. Patients suffering from Alzheimer's disease rely on four FDA-approved medications, none of which cure the disease. Furthermore the most recent approval was in 2003.[7] A fifth approved medication – tacrine – was discontinued in the US in 2013 due to concerns about safety.[8] Over 200 compounds targeting dementia have reached Phase II clinical trials since 2003, but in that time a cure – or even a new drug to treat dementia progression – has remained out of reach.[9] These failures have come at a price, as compounds that have been terminated from a company's late-stage pipeline can represent billions of dollars lost in R&D, which then impact the cost and pricing of approved drugs.

Much of the innovation in diabetes treatment has focused on developing long-term sensing devices and insulin delivery pumps to create an artificial pancreas. Additionally, a new class of products has recently been approved that combines long-acting insulin with GLP-1 receptor agonists (hormones that help normalise blood glucose levels).[10] With global diabetes incidence expected to increase by 55 per cent between 2015 and 2040, it is clear that numerous opportunities remain for biopharma to continue to innovate in diabetes treatment, including the potential for disease modification or cure.[11]

With the tidal wave of age and behaviour related non-communicable diseases growing, it is also important to remember the impact infectious disease has had on global public health. Prior to the twentieth century, an epidemic of one of many infectious diseases represented the biggest morbidity and mortality threat to a healthy population. Advances in treatments, such as antimicrobials and vaccines, alleviated the threat of many of these diseases, but new challenges are allowing infectious diseases to re-emerge as major threats to global public health, compounding the threat of the tidal wave.

Antimicrobial resistance may become the biggest threat to global public health in the twenty-first century. However, it also presents an opportunity for biopharma. For example, 480,000 people develop multi-drug resistant tuberculosis each year, and drug resistance is also becoming more prevalent in patients with HIV, malaria and influenza.[12] Similarly, recent outbreaks of diseases such as Ebola, Zika and others have highlighted the need for development of new vaccines and treatment options for infectious diseases. Despite these growing threats, most biopharma companies have either reduced or stopped altogether their R&D into new antimicrobials. Reasons for this include restrictions on product use and complexities in manufacturing that lower return on investment. Instead, biopharma companies are focusing on other therapeutic areas, such as cancer and chronic diseases.[13]

However, there is hope on the horizon for antimicrobials. Although not yet approved for human use, teixobactin is an antimicrobial in development that is part of the first new class of antimicrobials to be discovered since 1987.[14] Derived from microbes found in soil that had previously failed to grow under laboratory conditions, researchers developed an electronic device that mimics the natural habitat of these micro-organisms and isolates the antimicrobial chemical compounds they produce.[15] The search for new antimicrobials has also been boosted by new regulatory incentives, such as provisions in the 21st Century Cures Act that allow the FDA to simplify and expedite its approval processes,[16] and funding incentives, such as the Global Antibiotic R&D Partnership (GARDP), which recently raised €56 million to help develop new treatments to fight antimicrobial resistance.[17]

Across biopharma, high levels of unmet need remain. Confounding technical challenges in confronting the tidal wave of diseases demonstrate that new approaches will be required to have a significant impact on patients, although some of these approaches have already demonstrated promise.
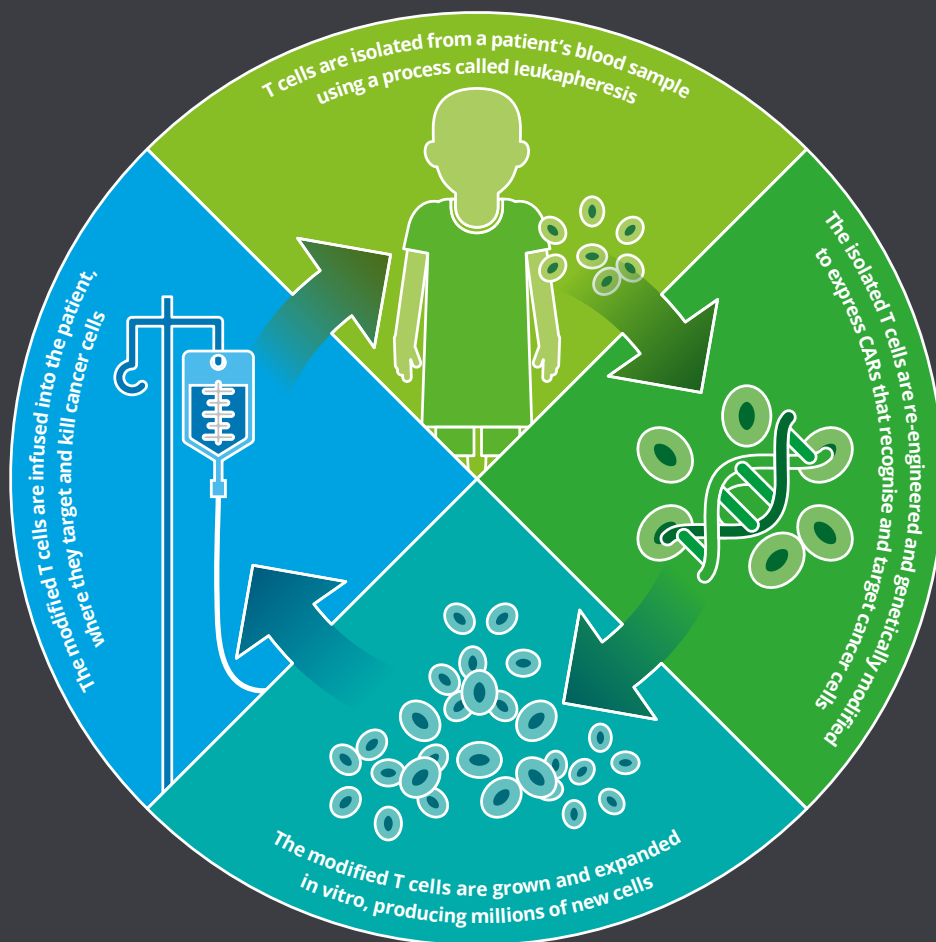
New platforms show promise in 2017
A number of promising platforms – like gene therapy – have potential to exert a pronounced impact on biopharma. For many of these platforms, the challenge will be scaling in an accelerated way across a company's portfolio.

Long predicted to be the future of medicine, gene therapy is becoming a reality. Although a treatment using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology has yet to receive regulatory approval, the technology has generated excitement around its potential for applications in biomedicine and beyond. Some of these potential applications include quickly creating cell and animal models to accelerate research into areas such as cancer and mental illness,[18] alleviating genetic disorders, expediting crop and livestock breeding, engineering new antimicrobials and controlling disease-carrying insects with gene drives.[19]

Another prominent new example of gene therapy is chimeric antigen receptor T cell (CAR-T) therapy, which uses a patient's own reprogrammed cells to target and kill cancer cells (see box below).

The first CAR-T therapies were approved in 2017

T cells are isolated from a patient's blood sample using a process called leukapheresis

The isolated T cells are re-engineered and genetically modified to express CARs that recognise and target cancer cells

The modified T cells are grown and expanded in vitro, producing millions of new cells

The modified T cells are infused into the patient, where they target and kill cancer cells

The first two CAR-T therapies, which use a patient's own reprogrammed cells to target and kill cancer cells, were approved by the FDA in 2017. These include:

- **Kymriah™ (tisagenlecleucel)** – to treat children and young adults with B-cell precursor acute lymphoblastic leukaemia that is refractory or in second or later relapse[20]

- **Yescarta™ (axicabtagene ciloleucel)** – to treat adult patients with certain types of B-cell lymphoma who have not responded to or have relapsed after at least two other kinds of treatment[21]

Using CAR-T to treat blood malignancies has led to response rates as high as 70-90 per cent, but the therapies are high-risk and are currently limited to specialised laboratories where clinicians are trained to handle adverse reactions that can be life threatening. Despite these risks, when successful, some patients experienced greater than one-year remission when treated with CAR-T therapy.[22]

The microbiome is also poised to have a significant impact on the biopharma industry in the near future. As we learn how to manipulate interactions between drugs and the trillions of microorganisms that live on and in the human body, we move closer to developing personalised therapies. One possible strategy for manipulation involves screening a patient's microbiome to determine if their specific makeup metabolises drugs before they have a chance to be effective. Preventing this unwanted metabolism by the microbiome could then be accomplished through changes in diet or prescription of a second drug, such as an enzyme inhibitor, which limits the microbiome's ability to metabolise the initial drug.[23] Currently, the complexity of microbiome-drug interactions has limited physicians' ability to prescribe these types of treatments routinely, but as our knowledge about the microbiome increases, so does the potential for new microbiome-based treatments.

Late 2017 also saw the approval of the first digital pill – a pill with an ingestible sensor that tracks whether a patient has taken a specific medication. The sensor is activated when it comes in contact with stomach acid and then links to a patch worn on the patient's ribcage, which in turn links to the patient's smartphone, allowing the patient to monitor and manage their medication usage. Data is sent to the patient's doctor and other care team or family members the patient nominates, with the aim of increasing adherence, which is particularly critical for patients suffering from chronic disease.[24]

Later in this report we will explore other examples of innovation in the industry and closely examine emerging technologies that have the potential to transform biopharma R&D, aiding in the advancement of drug development efforts and adding value to biopharma portfolios.

Measuring the return from pharmaceutical innovation

All of the reports in our series *Measuring the return from pharmaceutical innovation* focus on an original cohort of 12 large cap biopharma companies, and our three most recent reports also include an extension cohort of four mid-to-large cap biopharma companies. We use these cohorts as a proxy to measure the industry's ability to balance initial capital outlay with cash inflows biopharma companies are projected to receive as a result of this investment.

Methodology overview: A consistent approach to objective benchmarking

Our approach has maintained a consistent and objective methodology throughout the lifetime of our series that allows us to measure industry performance across the original and extension cohorts of companies. We use two inputs to calculate the Internal Rate of Return (IRR) from a company's late-stage pipeline: the total spend incurred bringing assets to launch (based on publicly available information from audited annual reports or readily available from third-party data providers) and an estimate of the future revenue generated from the launch of these assets. Figure 1 summarises our methodology, showing both the static and dynamic measures of R&D returns.

Our analysis accounts for multiple factors:

- forecast revenue splits where a particular compound is in development for multiple indications

- the impact of in-licensing and M&A on R&D costs

- success rates in late-stage development

- the impact of clinical cycle times.

Figure 1. Late-stage pipeline static IRR and drivers of change in IRR methodology
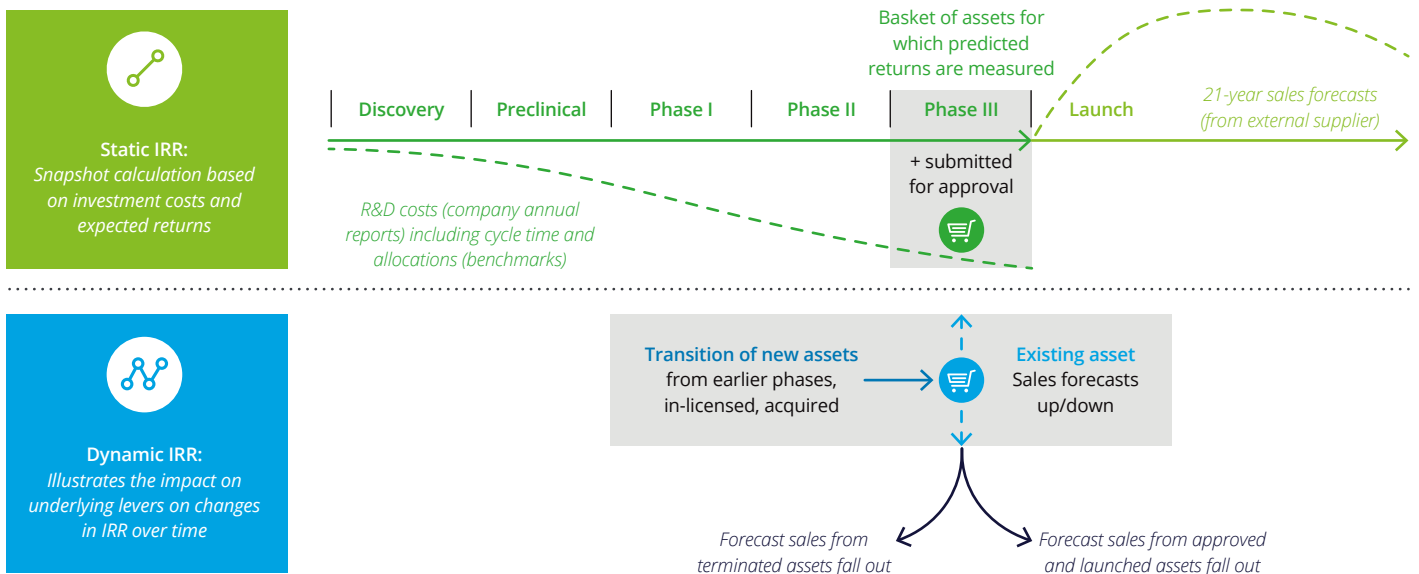
Source: Deloitte research, 2017

Given the inherent risks in undertaking R&D and the need to generate a complete view of R&D returns, our analysis also accounts for the cost of failure. Therefore, our calculations of the total spend incurred in developing and launching assets include the expenditure on terminated programmes and compounds. However, we limit our analysis to assets currently in late-stage development (Phase II breakthrough, Phase III and filed), which reduces our forecast risk to an acceptable level, as late-stage development contains a lower level of volatility than earlier phases of development.

We calculate the static year-on-year rate of return and also include the longer-term three-year average figure, which we first introduced in our 2015 report. This reduces the volatility associated with the static measures and provides a more well-rounded view of an organisation's projected R&D returns to match the long time periods over which decisions within R&D become impactful (see Appendix).

For the third year, we have also analysed the R&D returns of four mid-to-large cap biopharma companies (covering the period 2013-17). The inclusion of this extension cohort provides a greater understanding of their long-term performance and insight into factors linked to improved R&D productivity.

### The original cohort's projected returns decrease to 3.2 per cent

While the industry continues to innovate and deliver breakthrough therapies, the consolidated returns for the original cohort have continued to decline, with 2017 returns reaching only 3.2 per cent – a decrease of 0.5 percentage points from 2016 and a decrease of 6.9 percentage points overall from 2010 (see Figure 2). This corresponds to an average decline of nearly one percentage point per year, which does not bode well for the coming years.

Figure 2. Return on late-stage portfolio, 2010-17 – original cohort
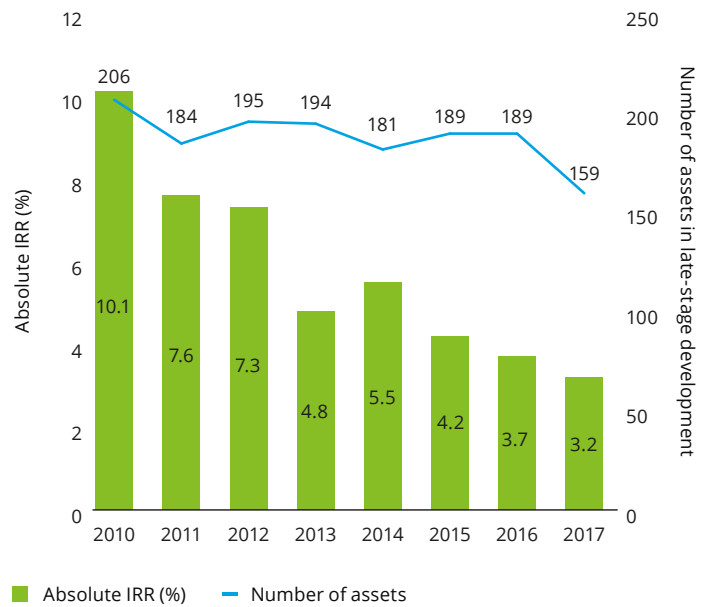
Source: Deloitte research, 2017

Figure 3. Return on late-stage portfolio, 2010-17 – original and extension cohorts
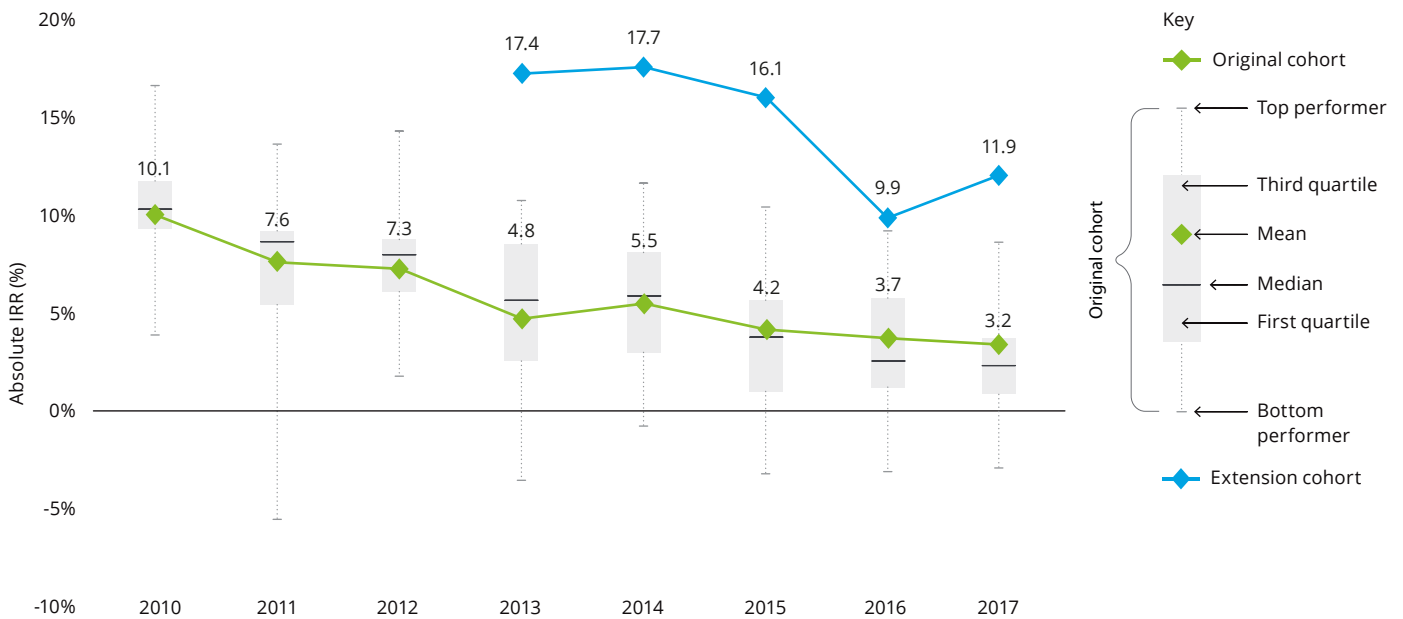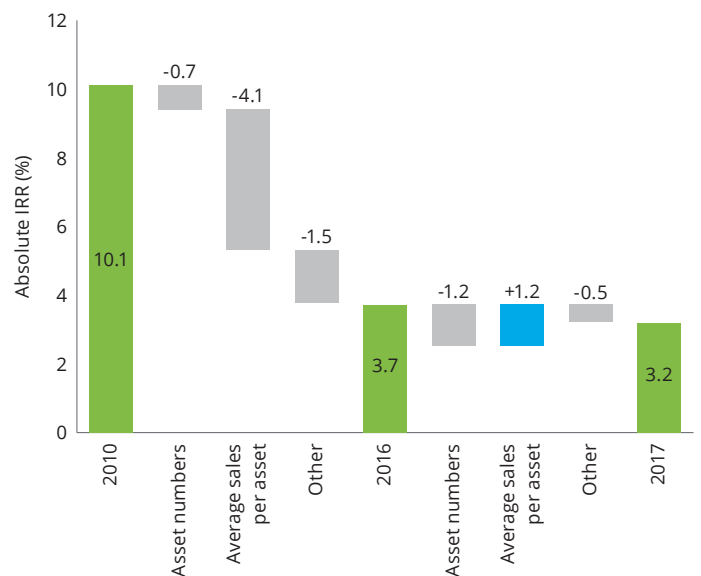

Source: Deloitte research, 2017

Variation within the returns of the original cohort of companies remains, although the range in values between the top and bottom performer is at its lowest point over the eight-year period (see Figure 3). Four of the 12 companies managed to improve their projected returns in 2017 compared to last year's analysis.

Previously, the number of assets in late-stage development remained relatively constant (191 ± 15, or an average of 16 per company from 2010 to 2016). The decline in returns was driven predominantly by the average forecast sales associated with the assets and increasing costs. However, 2017 saw a large decrease in the number of assets that are in late-stage pipelines to the lowest level we have seen in this series (see Figure 2). At 159, this is a decrease of 16 per cent from 2016 and a 17 per cent decrease from the average of the previous seven years. Consequently, the number of assets in late-stage development is the main driver of the decline in IRR in 2017 (see Figure 4). Trends underlying the decline in the number of assets are complex, but this correlates with the number of Phase III trials initiated during the reporting period (1 May 2016 – 30 April 2017) which, for the original cohort, decreased by 21 per cent.

Figure 4. Overall impact of pipeline factors on change in IRR, 2010-16 and 2016-2017 – original cohort

Source: Deloitte research, 2017

In a positive light, this could be a factor of researchers putting more emphasis on developing truly differentiated products that will improve standards of care and terminating less differentiated products early, rather than bringing them into late-stage pipelines and incurring significant associated costs. In a more negative light, this could reflect challenges that researchers are facing discovering and developing these assets.

Figure 5 shows the aggregate drivers of change for the original cohort between 2010 and 2017, referencing this to the year-on-year return on late-stage portfolio. It then illustrates the drivers of change between 2016 and 2017.

As assets are approved, forecast revenues move from the late-stage pipeline into the commercial portfolio and out of the scope of our analysis. During 2017, the 1.6 per cent decrease due to approvals was the lowest recorded for the original cohort since our analysis began in 2010. A total of 36 assets were launched by the original cohort between 1 May 2016 and 30 April 2017, transferring $119 billion in total sales to the commercial portfolio.

It was also a poor year for terminations, with late-stage failure the second largest factor in total IRR decline, corresponding to a decrease in returns of 0.7 percentage points. In this year's analysis, companies in the original cohort have been increasingly developing assets within smaller, more niche therapeutic areas (see our section on therapy area focus later in this report). These indications tend to be harder targets, and as such, success rates are lower for these therapeutic areas, thus explaining this year's sizeable decrease in returns due to terminations. This trend also partly accounts for the corresponding increases seen in cycle times and decreases in success rates, with companies investing their efforts in more risky therapeutic areas and indications. Companies may also be purposefully terminating assets that they deem unlikely to meet regulatory or reimbursement thresholds to be viable.

Core R&D costs have led to a decrease in returns of 0.6 percentage points, as companies continue to invest heavily in R&D, which corresponds to an increase of 4 per cent in the underlying R&D expenditure since 2016.

As noted earlier in the report, in 2017 there has been a decrease in the number of assets entering late-stage development. A total of 45 new assets entering pipelines contributed to an increase of 0.9 percentage points in projected returns, which is the lowest value we have seen in our *Measuring the return from pharmaceutical innovation* series. Commercialisation and terminations of previously existing late-stage assets have outpaced portfolio refresh, resulting in a decline in forecast returns for the original cohort. This has been a consistent trend across our series, with the increase in projected returns from new assets only outweighing decreases due to approvals and terminations in two of the periods.

On a more positive note, this is only the second time that the original cohort has been able to increase forecast inflows during late-stage development. This is in spite of the impact of de-risking, as assets pass through late-stage development. Previously, the factors likely to see an increase in forecast sales, such as class effect and competitor failure, have been outweighed by those that ameliorate the forecasts, such as negative trial data, new competitors emerging and increased generic erosion. During the past year, this has not been the case, and the ameliorating factors have been compensated for by positive trial data and trials generating data to expand the eligible patient population for indications currently in scope.

R&D operating margins have also continued to improve, with a modest increase of 0.2 per cent, suggesting that efforts within the industry to control costs are continuing to have a positive impact on projected returns.

Figure 5. Drivers of change in IRR, 2010-17 consolidated, 2010-17 year-on-year and 2016-17 – original cohort
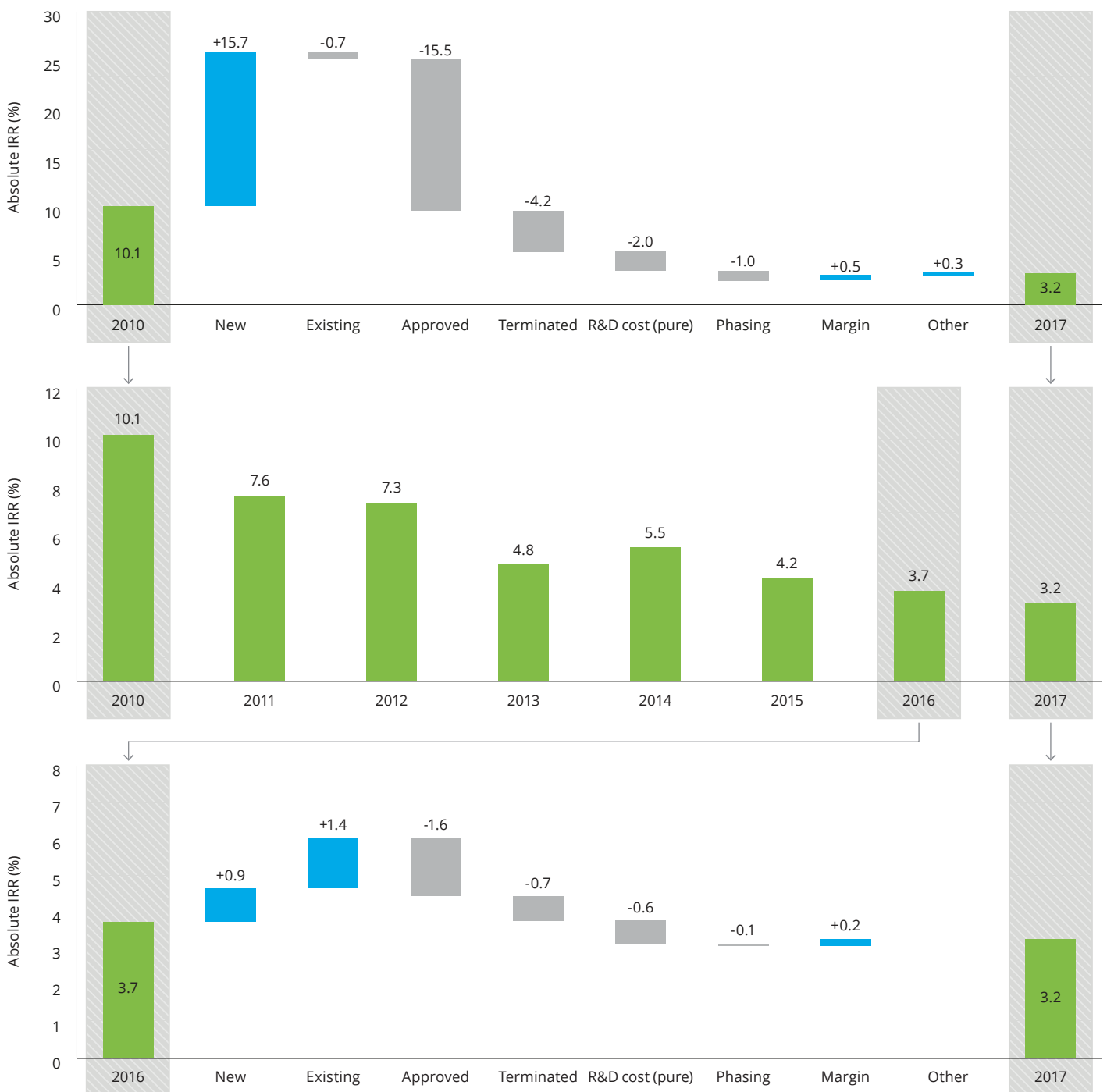
Source: Deloitte research, 2017

Figure 6. Drivers of change in IRR, 2016-17 – extension cohort

Source: Deloitte research, 2017

The extension cohort has seen a strong year of pipeline replenishment

Although the original cohort has seen a decline in IRR for the third consecutive year, the extension cohort has seen an increase in projected returns, from 9.9 per cent in 2016 to 11.9 per cent in 2017 (see Figure 3).

Our 2016 analysis identified strong commercialisation as the largest driver of change in IRR for the extension cohort due to the launch of nine assets, but 2017 has been a year of pipeline replenishment. Eight new assets that entered late-stage development contributed an increase of 5.7 percentage points in projected returns (see Figure 6).

While not as strong as last year, the extension cohort has still had a successful year of commercialisation in 2017, with the launch of five assets. This contributed to a decline of 2.0 percentage points in projected returns (see Figure 6). In addition to a decrease in forecast returns from assets released into the commercial portfolio, the extension cohort also saw a decrease in returns from existing pipeline assets of 1.8 percentage points.

This is in contrast to 2016, when 1.2 percentage points were added to its forecast returns, and it is the first time that the extension cohort has failed to add value to its late-stage pipeline since our analysis began. The primary drivers of this decline in existing pipeline value in 2017 were the emergence of new competitors/ positive competitor data and an increase in generic/biosimilar erosion. As with the original cohort, terminations also took their toll for the extension cohort, leading to a decrease of 1.1 percentage points, with a total of four assets leaving pipelines via termination.

As the extension cohort comprises a smaller number of companies than the original cohort, it is perhaps not surprising that there is more volatility year-on-year in the total number of assets entering and leaving late-stage pipelines.

The average cost to develop an asset continues to rise

There has been a significant increase in the average cost to bring an asset to market this year. For the original cohort, this cost in 2017 is $1,992 million, an increase of $453 million from 2016 (see Figure 7). This is largely due to the smaller number of assets currently in late-stage pipelines (159), which is used as the denominator in the calculation and is known to be relatively volatile. At a constant late-stage asset number (189 from 2016), this cost would have been $1,676 million, an increase of only $137 million. Another way of stabilising the volatility caused by the denominator is to use the three-year rolling average, which is tracking at $1,691 million for 2015-17 compared to $1,508 for 2014-16 (see Figure 19 in Appendix). This includes the cost of failure, impact of in-licensed and acquired assets, as well as internal R&D expenditure. Total long-term R&D expenditure for the original cohort has increased 12 per cent between 2010 and 2017.

The extension cohort has also seen an increase in its average cost to bring an asset to market, from $1,982 million in 2016 to $2,173 million in 2017. Again, this was largely driven by a decrease in the number of late-stage pipeline assets, despite a fall in biopharma R&D costs in 2017. Similarly, the three year rolling average R&D cost to develop an asset for the extension cohort increased from $1,381 million to $1,730 million (see Figure 19 in Appendix). Whichever metric is used, the cost to bring an asset to market is still high across both cohorts and continues to underline that the original cohort is not able to bring assets to market with sufficient efficiency to drive sustainable returns.

Peak sales per asset increase for both cohorts for the first time

Despite the decline in returns and decrease in overall number of assets in late-stage development, 2017 registers the first increase for the original cohort in average peak sales per pipeline asset since 2014. At $465 million, we saw an increase of $71 million from 2016 and a return to levels last seen in 2014 (see Figure 8). A total of three companies in the original cohort achieved a forecast peak sales per asset greater than $500 million in 2017, with 8 of the 12 companies improving their projected peak sales compared to 2016.

The extension cohort has moved back above blockbuster levels, with the average peak sales per pipeline asset at $1,128 million for 2017, which tops the previous high of $1,113 million achieved in 2015 (see Figure 8). Reasons for this include greater agility to pursue truly innovative assets and less need to replace large patent cliffs that are impacting commercial revenue streams.

However, it is still difficult for the original and extension cohorts to produce truly innovative assets, with both cohorts seeing a decline in the proportion of their late-stage pipeline revenue from first-in-class assets from 2014 to 2017. The original cohort has seen a decline from 65 per cent in 2014 to 48 per cent in 2017, with the extension cohort dropping from 85 per cent to 43 per cent over the same period. While companies are targeting more niche diseases and therapeutic areas, the associated risks are much higher, and as a result, companies are struggling to bring these compounds through their pipelines.

Figure 7. Average R&D cost to develop a compound from discovery to launch, 2010-17

— Extension cohort   — Original cohort
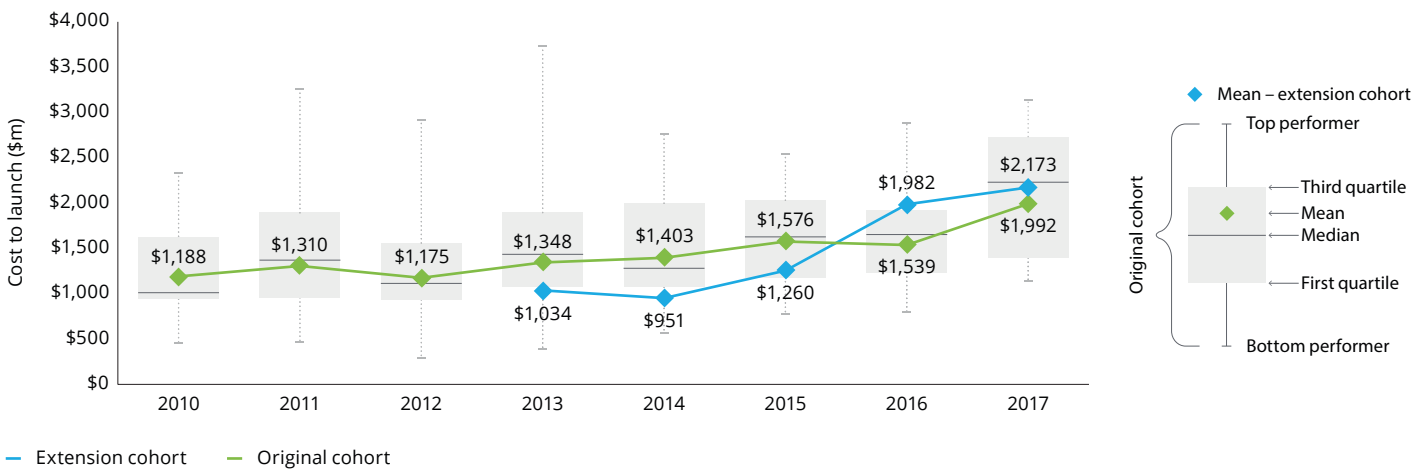
Source: Deloitte research, 2017

Figure 8. Average peak sales per pipeline asset, 2010-17

— Extension cohort   — Original cohort
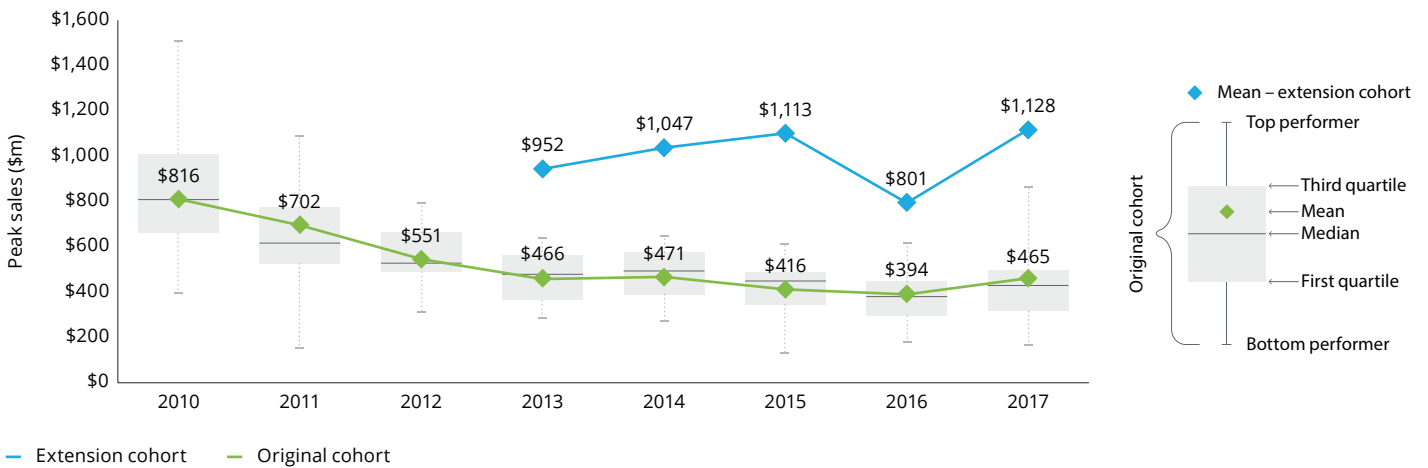
Source: Deloitte research, 2017

In search of innovation

This series focuses on measuring the financial return from pharmaceutical innovation. However, it would be a mistake to use these projected financial returns as the only measure of the industry's ability to innovate. Innovation itself can be broken into three broad themes: product innovation, innovation impacting the customer experience and technological innovation that enables the product to be delivered more efficiently. To provide some alternative context to the financial returns on innovation, it is useful to consider this in the context of quantitative measures of product innovation within the industry, such as new molecular entity (NME) and orphan drug approvals versus line extensions (LE).

NME approvals are a common metric to assess product innovation, as data is widely available from regulatory agencies. Using published data from the EMA and FDA to define product innovation from 2011 through to 2017 (coinciding with approvals since the first publication of this report), we see that NME approvals peaked in 2015, with 2016 seeing a decrease (see Figure 9). However, the projected full-year totals for 2017 suggest the number of approvals is likely to be on par with 2014 and above the average for the seven years considered.

After a dip in NME approvals last year for our two cohorts, this year (up to September) has already seen approvals surpass last year's total, and additional approvals in the final few months of the year may increase these numbers even more. A projected increase in NME approvals this year aligns with the increased strategic focus of our cohorts of targeting more niche therapeutic areas. While this forecast increase demonstrates that companies in our cohorts are improving their ability to bring NMEs to market, this focus has also had an increased impact on product terminations this year due to the lower associated success rates. However, approval numbers for our cohorts are still likely to be below those from 2014 and 2015.

NME approval numbers are not a holistic measure of the state of innovation. However, this can be enhanced by using measures of innovation quality. Figure 10 tracks the percentage of forecast peak sales of launch products and pipeline assets (both NMEs and indication expansions) that are from first-in-class treatments and those with an orphan/breakthrough/fast-track designation within our 16 focus companies, combining this with commercial value.
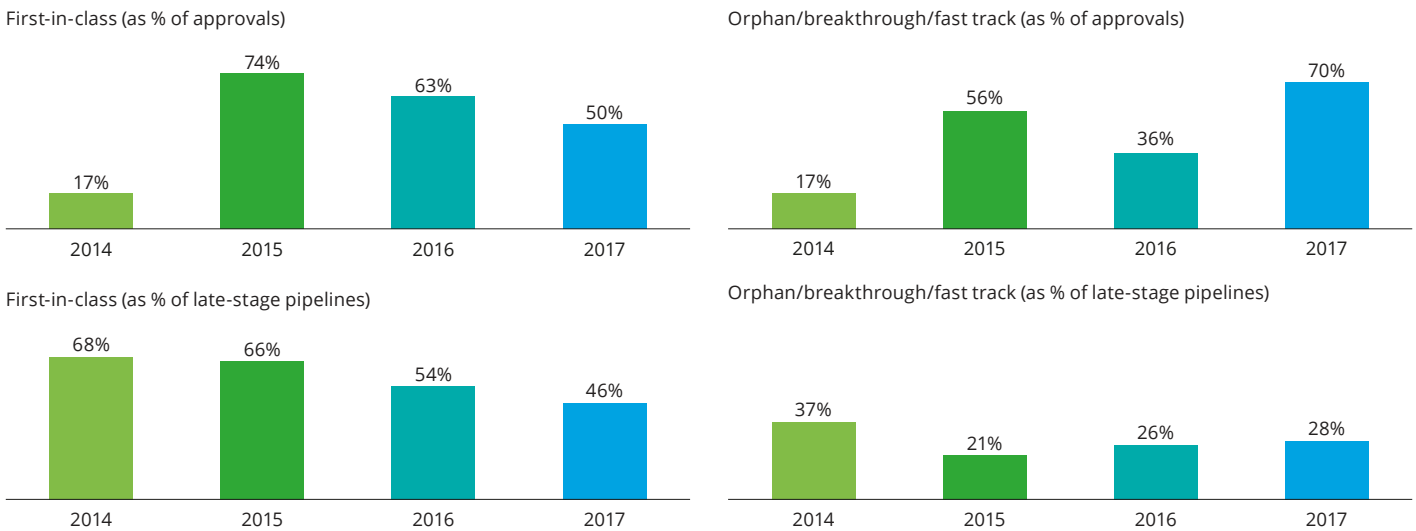
Figure 9. Number of NME approvals, 2011-17
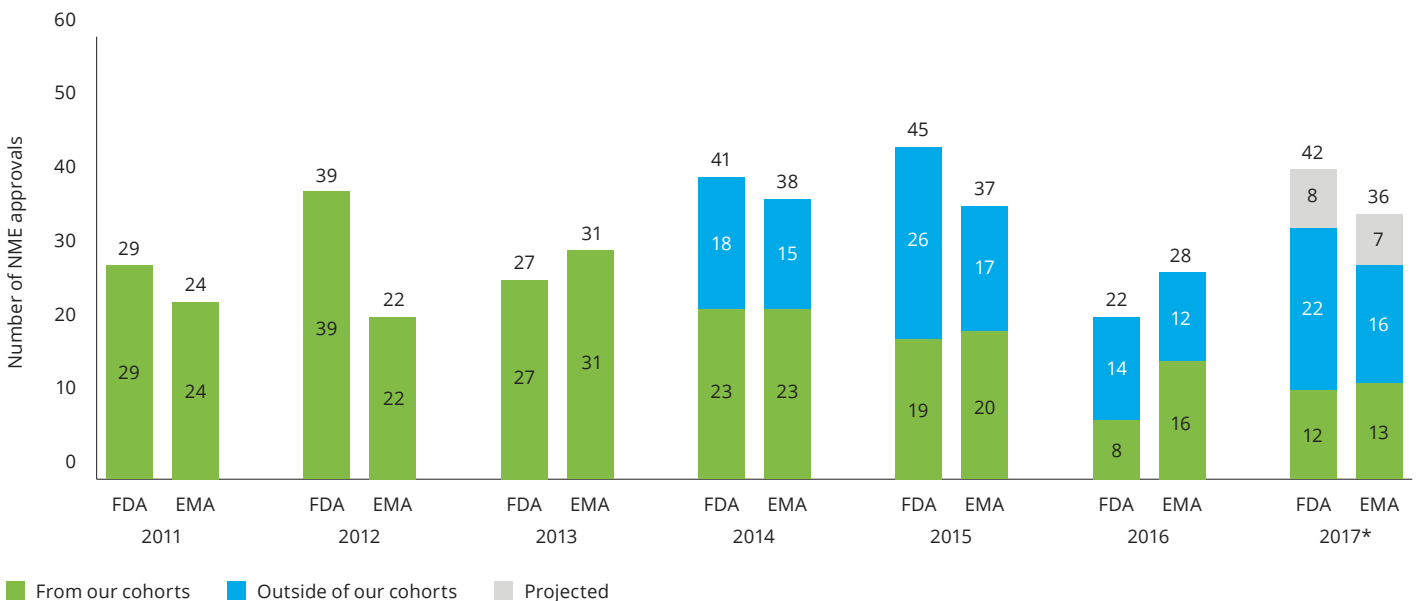
*includes projected figures as the analysis was performed prior to the end of the year.

Source: Deloitte research, 2017

Figure 10. Per cent of total peak sales from pipeline products and launch assets that are first-in-class and with orphan/ breakthrough/fast-track designation

First-in-class (as % of approvals)

	2014	2015	2016	2017
	17%	74%	63%	50%

Orphan/breakthrough/fast track (as % of approvals)

	2014	2015	2016	2017
	17%	56%	36%	70%

First-in-class (as % of late-stage pipelines)

	2014	2015	2016	2017
	68%	66%	54%	46%

Orphan/breakthrough/fast track (as % of late-stage pipelines)

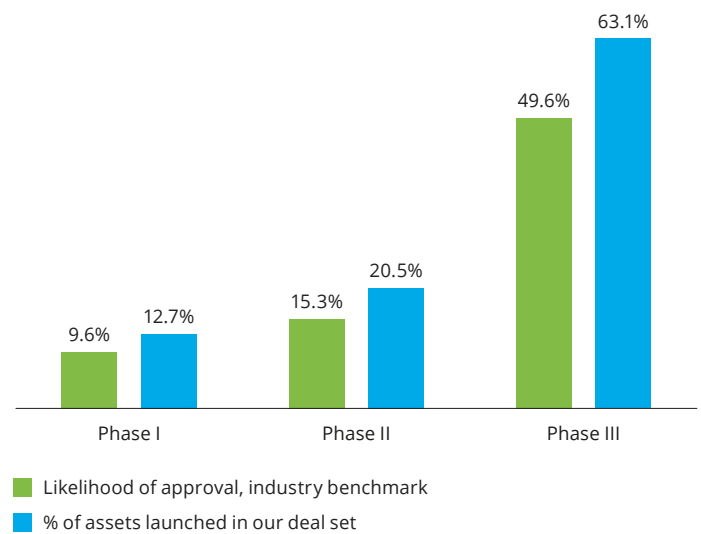|	2014	2015	2016	2017
	37%	21%	26%	28%

Source: Deloitte research, 2017

The percentage of forecast peak sales coming from first-in-class approvals has declined since 2015. However, at 50 per cent in 2017, this continues to represent a significant proportion of projected sales from our 16 companies. The percentage of first-in-class in late-stage pipelines has shown a similar trend. Conversely, the percentage of projected sales from approved drugs with orphan/breakthrough/fast-track designations has been on an upward trajectory, representing over 70 per cent of total peak sales of approved products in 2017. Orphan/breakthrough/fast-track designations in the late-stage pipeline have also followed this trend. This demonstrates that innovation in biopharma is contributing significant patient value, as those with limited or no treatment options gain access to effective therapies.

This product innovation needs to be delivered in a sustainable way. Configuration in the form of partnerships and collaborations is increasingly recognised as a more efficient way to innovate, as discussed in Deloitte's report *External innovation: How biopharma companies are bolstering R&D pipelines through deal-making*.[25] This report illustrated that launch rates among externally sourced drugs are consistently higher than the industry benchmark noted by Biomedtracker, which analyses the likelihood of approval (LOA) for internally developed and externally sourced drugs across therapeutic areas (see Figure 11). This is likely to be primarily due to the selection of de-risked assets with promising data. It is also worth noting that this does not reflect the cost incurred to make these deals, which are becoming increasingly expensive.

Figure 11. Externally sourced assets' launch rates are higher than industry benchmarks

	Phase I	Phase II	Phase III
Likelihood of approval, industry benchmark	9.6%	15.3%	49.6%
% of assets launched in our deal set	12.7%	20.5%	63.1%

■ Likelihood of approval, industry benchmark
■ % of assets launched in our deal set

Source: External | innovation: How biopharma companies are bolstering R&D pipelines through deal-making. Deloitte LLP, 2017.
See also: https://dupress.deloitte.com/dup-us-en/industry/health-care/ biopharma-companies-deals-research-development.html

Therapy area focus has changed for our original cohort since 2010

We are seeing evidence in our data that the biopharma companies from the original cohort have shifted their focus on specific therapeutic areas as they look to maximise their return on investment in R&D. Products targeted at therapeutic areas such as CNS (central nervous system) and oncology are associated with higher pricing, and our analysis suggests that companies are targeting these therapeutic areas (TAs) with increasing prevalence. However, these TAs are also associated with lower success rates and a lower likelihood of making it to market, so this strategy is associated with higher levels of risk.

From 2010-17 the percentage of forecast late-stage pipeline revenue from oncology has increased significantly, from 18 per cent in 2010 to 37 per cent in 2017, whereas forecast revenue from CNS has remained relatively constant (6 per cent in 2010 to 7 per cent in 2017). However, if we consider the extremely high attrition rates within Alzheimer's disease alone, the lack of movement within CNS is perhaps less surprising. Conversely, the proportion of late-stage forecast sales from cardiovascular therapies has declined significantly, from 18 per cent in 2010 to just 3 per cent in 2017. Similarly, therapies for metabolic disorders have declined to just 9 per cent of forecast revenue, down from 15 per cent in 2010 (see Figure 12).

Where is the innovation?

Our 2017 analysis is a stark reminder that investing in biopharma R&D is risky, and financial returns are by no means guaranteed. Despite the decrease in returns for the original cohort, we see positives in the increase in forecast peak sales per asset, as companies increasingly target areas of unmet medical need and/or rare disorders. The ability of the original cohort to improve its projected returns from existing late-stage pipeline assets also represents an improvement from last year.

The extension cohort's pipeline replenishment and successful year of commercialisation also shows promise, as it resulted in an uptick in IRR back above ten per cent, although this is still significantly lower than results from 2013-15. Overall, the extension cohort continued to outperform their larger counterparts from the original cohort, continuing the negative correlation between company size and IRR that we have seen in previous years.

The next section will explore technological innovation the industry could use to drive efficiency, replenish pipelines and ultimately bend the cost curves that haven't changed significantly since our series began.

Figure 12. Late-stage pipeline composition by TA, 2010-17 – original cohort
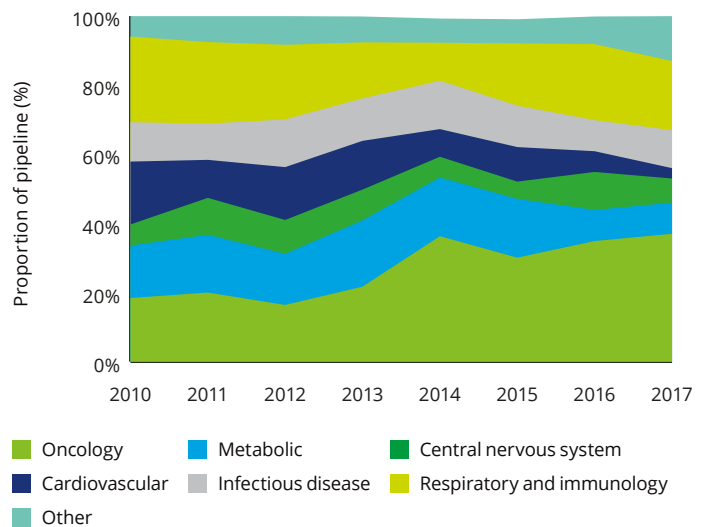
Source: Deloitte research, 2017

Applying emerging technologies to improve R&D productivity

The near future will bring numerous transformational changes to how entire industries function, including biopharma. The Deloitte Insights report *Navigating the future of work* explores three main forces shaping the nature of the future of work and the future workforce: technology; demographics; and 'the power of pull' – the ability to find and access people and resources when and as needed.[26] Of these, we anticipate technology will have the largest impact on biopharma R&D.

Adoption of new technology will result in a leaner operating model that will deliver more cost-effective medical innovations. The transition to this operating model, which we refer to as industrialisation, forms the basis for one of the predictions in the Deloitte report *The future awakens: Life sciences and health care predictions 2022*.[27] If biopharma is to make this transition, its biggest hurdle will be in lowering R&D costs, which have increased since we started tracking them in 2010. Therefore, this year's qualitative analysis focuses on ways in which innovative technologies can increase the productivity and efficiency by which drugs are discovered, developed and brought to patients.

Biopharma companies are just starting to experiment with these technologies, forming innovation teams and funding pilots. There are operational, cultural, and data accessibility/interoperability challenges in scaling up the adoption of the technologies, but early adopters will reap the rewards of a much more efficient R&D process, improving both the quality of assets and the time and cost it takes to get them to market. The following sections describe emerging technologies that could be applied across the value chain and result in a transformative improvement in IRR.

AI to improve efficiency in drug discovery

As our understanding of the capacity and capability of artificial intelligence (AI) has increased, a growing number of global biopharma companies are turning to AI in a bid to streamline the drug discovery process. AI algorithms can analyse large data sets from sources such as clinical trials, health records, genetic profiles and pre-clinical studies; within this data, it can recognise patterns and trends and develop hypotheses at a much faster rate than researchers alone. For example, using the vast array of information on drug compounds and test results that exist within biopharma, AI has the potential to assess this information rapidly, in conjunction with researchers, to help facilitate drug discovery and develop new insights faster.

Using AI for screening new drugs is also a possibility. The traditional method used by biopharma of screening large numbers of compounds and molecules for potential candidates is a lengthy and expensive process. AI could potentially carry out this process in a shorter period of time, and for less cost, as it is able to classify drugs into categories of therapeutic use with a high degree of accuracy. Even the incorrect answers AI provides could prove useful, as they might identify secondary uses for drugs that scientists would not have considered.

AI to improve study design and decision-making

In biopharma, data resides in multiple places, often from more than one source, making analysis and utilisation a major challenge. AI has several applications to help navigate vast data sets in clinical trials.

Effectively tracking clinical trial recruitment and enrolment
Digital platforms are helping to accelerate clinical trial patient recruitment, utilising AI to identify potential candidates through targeted advertising. Once patients are recruited, machine-learning can boost enrolment by studying why patients accept or decline invitations to relevant studies. AI can also greatly reduce the time and resources it takes to extract meaningful patient data from an electronic medical record (EMR). It can use data from historical cases, help companies measure responses to drugs, predict performance of certain trial sites, predict drop outs, and in some cases help predict outcomes. This information can help companies improve recruitment, decide to adjust trial criteria, or modify data collection methods.[28]

Identifying drivers of value in patient engagement
Many in biopharma are increasingly focused on how they can use data to give patients and consumers a better experience – be it enrolling in clinical trials, finding out more about how different patients experience their disease and what is most important in their treatment, and in figuring out how to help patients adhere to a medication regimen. AI has the potential to help biopharma better curate the patient experience.

Adherence in clinical trials

Low adherence in clinical trials can undermine measured health outcomes. Around 20-30 per cent of clinical trials fail because of non-adherence, and companies are looking for technology and solutions to help reduce that number. An AI company called AiCure provides advanced facial recognition solutions in an app that monitors medication adherence for diseases that require high levels of adherence. The technology is being used to monitor study participants in clinical research to help sponsors determine if patients are following protocols.[29]

Centralised and real-time clinical trial monitoring

Because biopharma companies have huge amounts of data, some traditional processes may be inefficient at providing a clear picture of all the data different teams may need to make decisions. Rarely is there a central portal to make sense of certain information quickly, such as progress updates from several different laboratories or clinical trial sites. Some companies are moving towards having a central source or portal. AI could enable companies to benefit from the rapid gathering and organising of vast quantities of data. AI could also help companies analyse large amounts of operational data from historical cases, predict performance of different clinical trial sites, and use predictive criteria to determine drug outcomes, drop-out rates and success rates of trials.
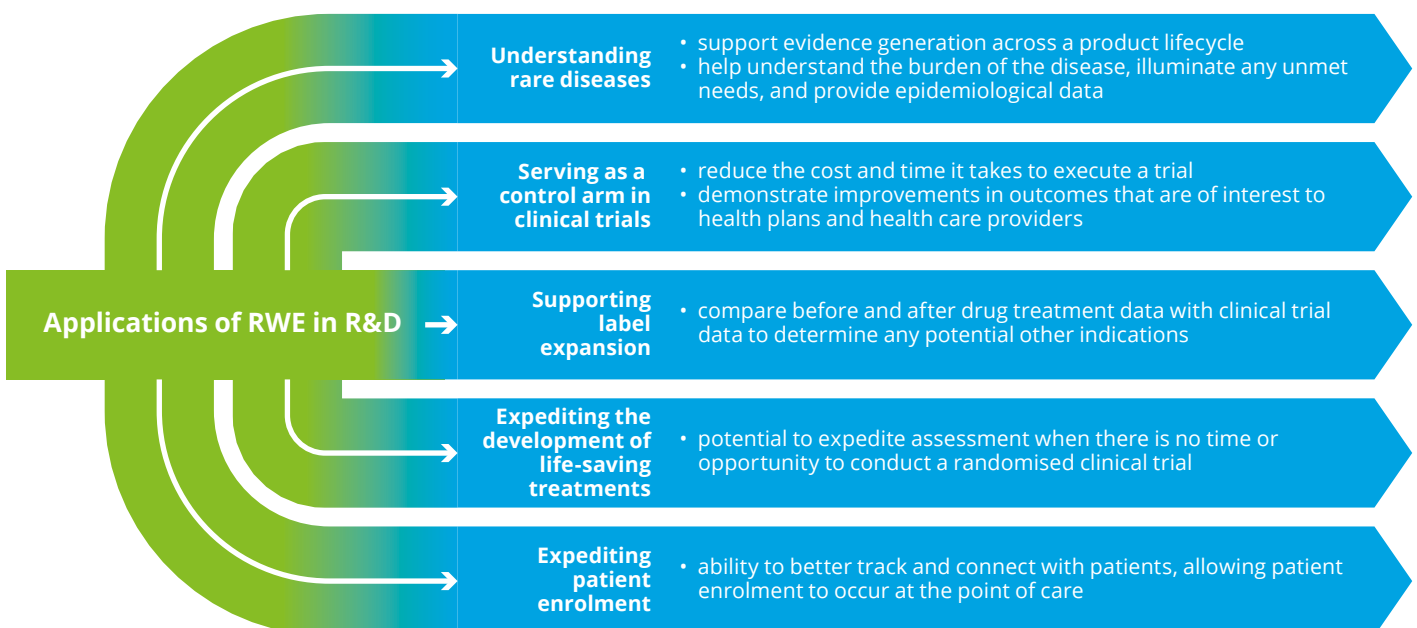
Harnessing real-world evidence to improve R&D productivity

Real-world evidence (RWE) is helping to revolutionise the way biopharma companies evaluate new therapies for safety and effectiveness. The use of RWE could also reduce the time it takes to recruit patients, identify subpopulations and to conduct research, and in many cases it could make drug development and approvals more efficient. RWE has several applications in biopharma R&D (see Figure 13).

Deloitte's 2017 RWE benchmarking study, *Getting real with real-world evidence*, found that biopharma companies are starting to invest in RWE capabilities and are exploring a number of use cases. More than half (54 percent) of the leaders who responded said they are putting money into RWE programmes to boost their capabilities significantly.[30]

Embracing RWE as a tool to demonstrate effectiveness beyond the clinical trial setting can help biopharma companies provide evidence on improved patient outcomes and improve health care system efficiencies, which in turn can support market value propositions and potentially increase IRR.

Figure 13. Applications of real-world evidence in R&D

Applications of RWE in R&D

Understanding rare diseases
- support evidence generation across a product lifecycle
- help understand the burden of the disease, illuminate any unmet needs, and provide epidemiological data

Serving as a control arm in clinical trials
- reduce the cost and time it takes to execute a trial
- demonstrate improvements in outcomes that are of interest to health plans and health care providers

Supporting label expansion
- compare before and after drug treatment data with clinical trial data to determine any potential other indications

Expediting the development of life-saving treatments
- potential to expedite assessment when there is no time or opportunity to conduct a randomised clinical trial

Expediting patient enrolment
- ability to better track and connect with patients, allowing patient enrolment to occur at the point of care

Source: Deloitte research, 2017

Robotic and cognitive automation can increase efficiency and accuracy of repetitive tasks

Robotic and cognitive automation (RCA) can enable cost efficiency, productivity gains and quality/compliance improvements in clinical trials. Automation of certain aspects of the clinical trial process could free up programme teams to focus on critical path activities, or accomplish tasks that were previously considered too time consuming or costly.

RCA could also be applied across the clinical trial value chain. Most clinical trial deliverables involve either data or documentation, creating numerous opportunities to use RCA to automate work and streamline resources. For example, RCA could expedite site selection by generating a first draft informed consent, identifying potential investigators using RWE sources, and making updates to the site and investigator profile database. RCA could support site initiation by collecting standard initiation documentation (such as investigator CVs, medical licenses and financial disclosures) and generating first draft site contracts and training. Site monitoring could also be improved by RCA, which can generate a first draft of site visit reports and quality control those visit reports.

Beyond automation, some cognitive technologies can provide insight and expedite report writing, such as Natural Language Generation (NLG). For example, NLG can expedite the creation of dossier submissions by automating the safety and efficacy sections, freeing up medical writers to focus on higher value work. NLG can evaluate patient demographics and thousands of lines of adverse event reports from a clinical trial to generate patient narratives included in the final clinical study report (CSR). This application of NLG reduces time spent on repetitive reporting, improves consistency of communication, reduces compliance risk and ultimately reduces time to market.

Other digital technologies can help drive greater patient engagement and improve data quality in clinical trials

Patient engagement has become an important topic of discussion in biopharma over the last few years, spurred on by regulatory and industry activity, including a number of public-private partnerships (see sidebar). The value of increased patient engagement is well understood in terms of the impact on improving the patient experience in clinical trials and in managing their condition, but it can be difficult to quantify in terms of return on investment. The Clinical Trials Transformation Initiative (CTTI) published a study that estimates the value of increased patient engagement in terms of expected net present value (ENPV) for an oncology programme going into Phase II or III. The authors estimate that increased patient engagement for a pre–phase II project that avoids one protocol amendment and improves trial enrolment, adherence and retention could increase net present value (NPV) by $62 million and increase EPNV by $35 million.[31]

The FDA is encouraging innovation in clinical models

Reliance on patient experience and RWE are themes that are woven throughout the 21st Century Cures Act, a bipartisan US law that was enacted in December 2016. Under the law, the use of patient experience data and other drug development tools will help bring drugs to market more quickly by streamlining clinical trials. As part of the Act, the FDA is in the process of working with multiple stakeholders to develop a regulatory framework to evaluate RWE in the drug (and device) approval process. Currently, the FDA has some guidance to help companies understand how it is using RWE when considering the expanded use of existing medications.

The FDA's Innovation Initiative
In addition to this recent legislation, the FDA has been outspoken about its desire to evaluate innovation in clinical trials. For example, leadership has written about the use of in silico tools in clinical trials for improving drug development and making regulation more efficient. In silico models use computer simulations to predict clinical outcomes, inform clinical trial designs, support evidence of effectiveness, optimise dosing, predict product safety, and evaluate potential adverse event mechanisms.

In addition, the creation of natural history databases could support model-based drug development. These databases could help to evaluate new treatments for rare diseases, or simulate a control arm in clinical trials. FDA is collaborating to develop such models in Parkinson's disease, Huntington's disease, Alzheimer's disease, and muscular dystrophy.[32]
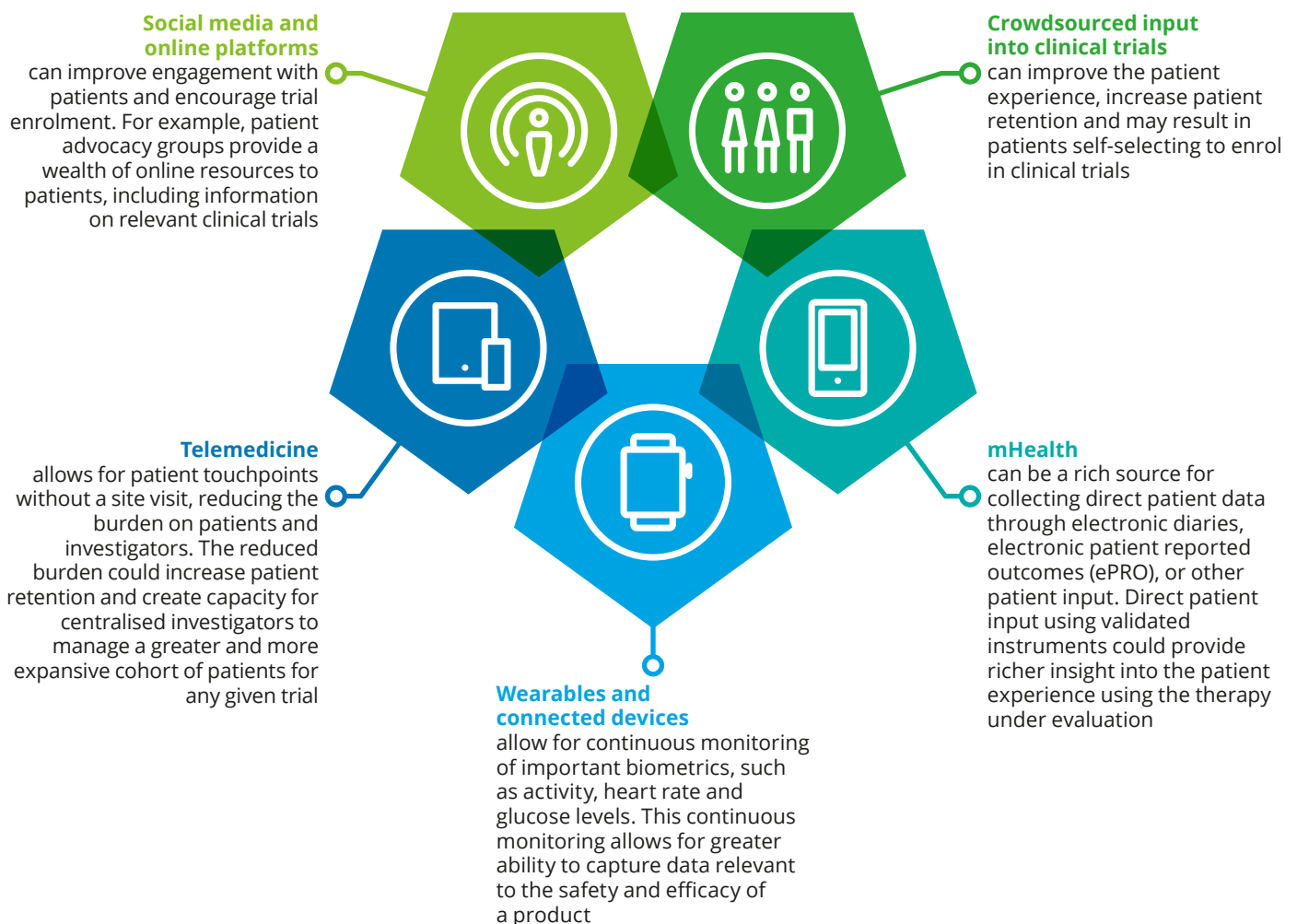
Encouraging collaborative clinical trial approaches
The FDA has encouraged greater industry participation in collaborative clinical trials, or trials that leverage master protocols and allow for continuous evaluation of multiple interventions, biomarkers, and outcomes. These studies leverage a combination of RWE and interventional observations, and would be a welcome source of data by the agency. FDA authors wrote an article in the New England Journal of Medicine that summarizes the potential benefits of these types of clinical trials.[33]

Technologies such as social media, mHealth, wearables, connected devices, and telemedicine all have the potential to transform how patients engage in clinical trials, enabling expedited enrolment, adherence, retention and improvements in study design and data quality. These technologies used in combination could reduce or even eliminate the need for physical sites, reducing the burden on patients but also on companies and investigators. The concept of site-less trials envisions a future where patients can be enrolled through an online platform, monitored via telemedicine visits, with data collected through apps, wearables, and connected devices, and visiting nurses traveling to patient homes to collect bio-specimens. These technologies could provide numerous benefits to patient engagement and clinical trial productivity, even when used independently (see Figure 14).

Digital technologies can also enable the creation of digital biomarkers, or consumer-generated physiological or biological measures collected through connected digital devices.[34] Digital biomarkers have the potential to improve the quality of data that is collected, through better sensitivity or less variability compared to older, manual instruments. For example, a connected device could enhance the ability to measure gait and balance in patients with Parkinson's disease. This improvement in sensitivity could reduce the number of patients that need to be enrolled in a clinical trial. Benefits also include greater adherence and patient engagement.

Figure 14. Technologies that can benefit patient engagement and clinical trial productivity

Social media and online platforms
can improve engagement with patients and encourage trial enrolment. For example, patient advocacy groups provide a wealth of online resources to patients, including information on relevant clinical trials

Crowdsourced input into clinical trials
can improve the patient experience, increase patient retention and may result in patients self-selecting to enrol in clinical trials

Telemedicine
allows for patient touchpoints without a site visit, reducing the burden on patients and investigators. The reduced burden could increase patient retention and create capacity for centralised investigators to manage a greater and more expansive cohort of patients for any given trial

mHealth
can be a rich source for collecting direct patient data through electronic diaries, electronic patient reported outcomes (ePRO), or other patient input. Direct patient input using validated instruments could provide richer insight into the patient experience using the therapy under evaluation

Wearables and connected devices
allow for continuous monitoring of important biometrics, such as activity, heart rate and glucose levels. This continuous monitoring allows for greater ability to capture data relevant to the safety and efficacy of a product

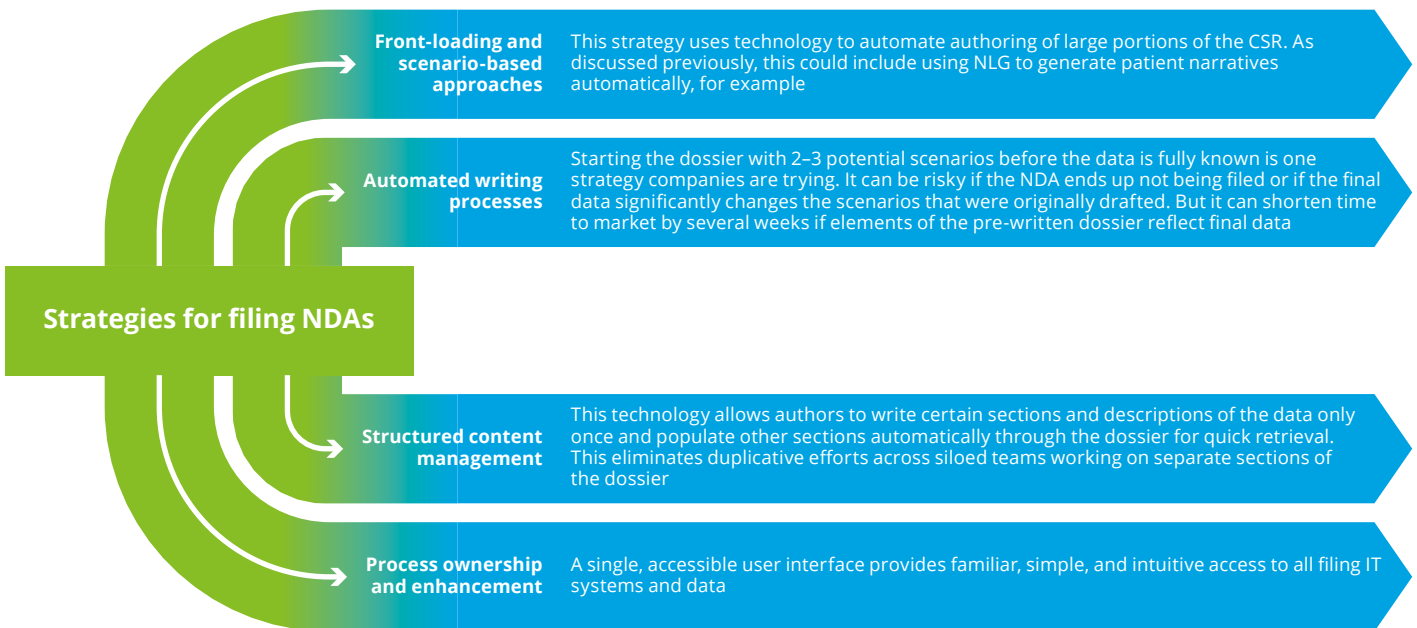Source: Deloitte research, 2017

Technologies can be used to file NDAs faster and at lower cost

Many companies are exploring ways to make the process of filing for a New Drug Application (NDA) – or the dossier that contains all the technical data of the biopharma product to be approved and marketed – easier, faster and less expensive. The FDA reports that median approval times for priority NDAs is eight months, or around 240 days.[35] This means some companies are taking as many as 300 or 400 days to get their drug application filed, before it can be approved and marketed. Companies that are not looking for ways to speed up this process, without compromising on quality or leading to staff burnout, risk falling behind the companies that are starting to use faster, less expensive strategies (see Figure 15).

There are both transformational and more routine operational strategies biopharma companies can apply to achieve faster filing. Deloitte research indicates that saving 12 weeks off filing time could generate additional NPV of $800 million to a biopharma company with a balanced portfolio, by accelerating time to market for filings expected to be submitted next year. Companies should consider exploring their use of technology, operational processes, and use of talent to achieve the goal of faster filing.

Figure 15. Strategies for filing NDAs faster and less expensively

Strategies for filing NDAs

Front-loading and scenario-based approaches
This strategy uses technology to automate authoring of large portions of the CSR. As discussed previously, this could include using NLG to generate patient narratives automatically, for example

Automated writing processes
Starting the dossier with 2–3 potential scenarios before the data is fully known is one strategy companies are trying. It can be risky if the NDA ends up not being filed or if the final data significantly changes the scenarios that were originally drafted. But it can shorten time to market by several weeks if elements of the pre-written dossier reflect final data

Structured content management
This technology allows authors to write certain sections and descriptions of the data only once and populate other sections automatically through the dossier for quick retrieval. This eliminates duplicative efforts across siloed teams working on separate sections of the dossier

Process ownership and enhancement
A single, accessible user interface provides familiar, simple, and intuitive access to all filing IT systems and data

Source: Deloitte research, 2017

Collaborative models use shared resources to expedite development and trials

The cost and complexity of drug discovery is also leading many biopharma companies to partner with academia, public research institutes, private foundations, tech companies and other biopharma companies to speed up the development of new drugs (see below).
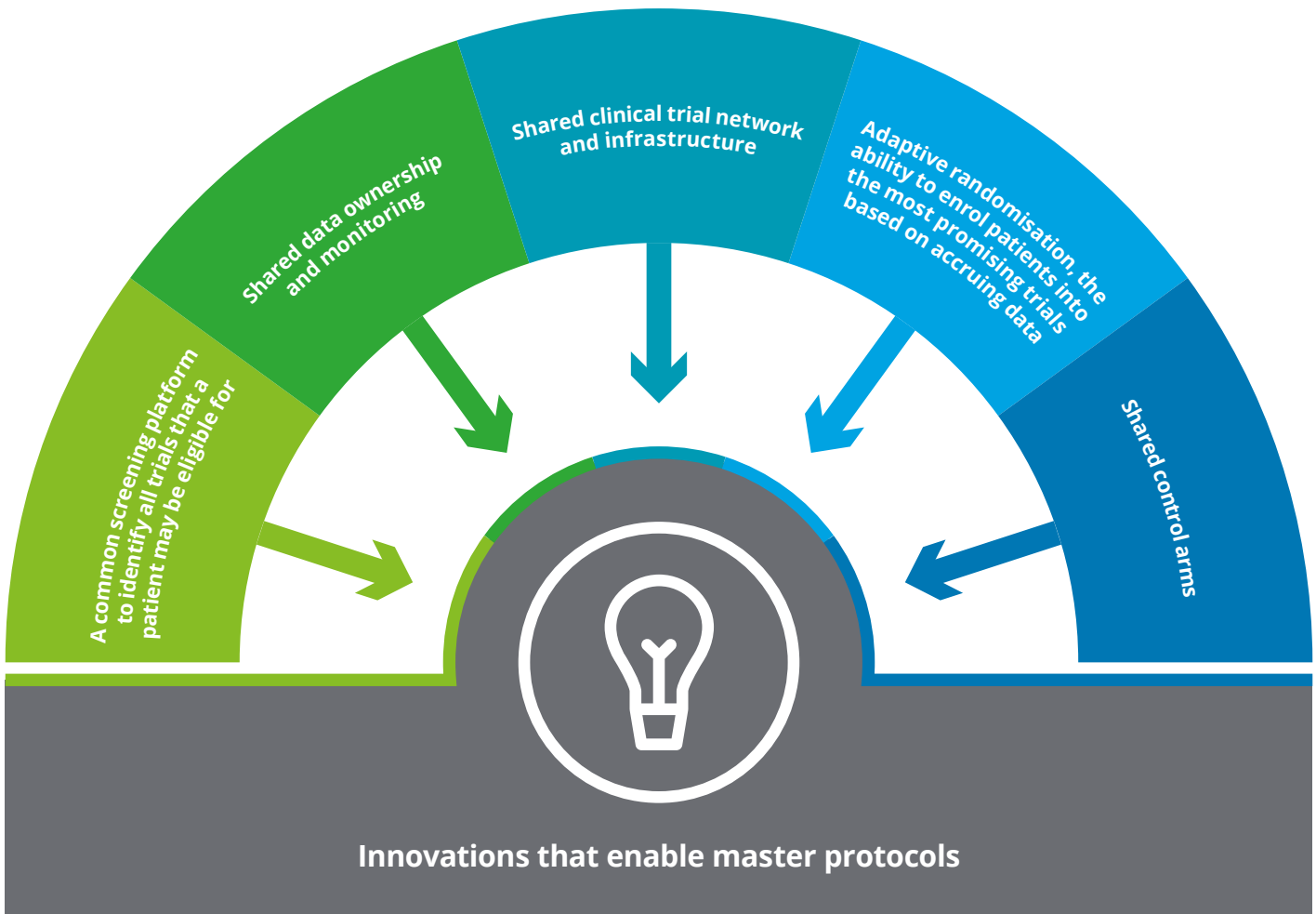
Improving the efficiency of drug discovery and development through partnerships – The Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) is the world's largest public-private partnership in the life sciences. IMI supports collaborative research projects and builds networks of industrial and academic experts in Europe, with the aim of boosting innovation in health care by constructing a more collaborative ecosystem for biopharma R&D.[36] For example, IMI's GetReal project aims to develop new ways of incorporating real-life clinical data into drug development. The project analyses existing methodologies and processes for health technology assessment (HTA) and also generates a decision-making framework to help companies design drug development strategies. The project creates a network of key stakeholders from industry, academia, regulatory agencies, HTA bodies, reimbursement agencies, health care budget holders, and patient groups to share their insights and expertise and help develop a consensus on best practice in the timing, performance and use of real-life studies in regulatory and reimbursement decision making. The programme not only allows biopharma companies to make better decisions during drug development, it also allows health care decision-makers to decide how best to grant patients access to new treatments.[37]

In conducting clinical trials, companies traditionally create infrastructure focused on one drug treatment at a time. The pursuit of more complex disease areas and targeted therapies focused on narrower populations has made this approach unsustainable. Some companies may struggle to find sufficient patients to study new therapies, extending development timelines and reducing R&D efficiency. This is becoming increasingly challenging in oncology, where multiple companies are developing drugs and testing combination therapies for similar populations.[38]

Novel clinical trial designs that employ master protocols could provide a more patient-centric solution. These trial designs investigate multiple treatments (targeted or otherwise) in parallel, for one or more diseases. This allows the investigation of combination therapies or the analysis of patient sub-groups using shared infrastructure. These trial designs could also include a common control arm and allow new investigational protocols to be added or removed if not efficacious.[39] Master protocols are enabled by a number of innovations (see Figure 16).

**Figure 16. Innovations that enable master protocols**

Shared clinical trial network and infrastructure

Shared data ownership and monitoring

Adaptive randomisation, the ability to enrol patients into the most promising trials based on accruing data

A common screening platform to identify all trials that a patient may be eligible for

Shared control arms

Innovations that enable master protocols

Source: Woodcock J and Lavange LM. Master protocols to study multiple therapies, multiple diseases, or both. New England Journal of Medicine, 6 July 2017

Our results show that the biopharma industry continues to face an incredibly challenging R&D environment and has yet to turn a corner in terms of its value proposition. However, we have also seen some room for optimism, due to improvements in the efficiency of certain R&D processes and the adoption of new technologies. Biopharma companies are just starting to experiment with these technologies, and there are operational, cultural, and data accessibility/interoperability challenges in scaling up adoption. However, early adopters will reap the rewards of a much more efficient R&D process, improving the quality of assets and the time and cost it takes to get them to market, which taken together could have a transformative impact on IRR.

Appendix

Figure 17. Year-on-year drivers of change in IRR, 2010-17 – original cohort
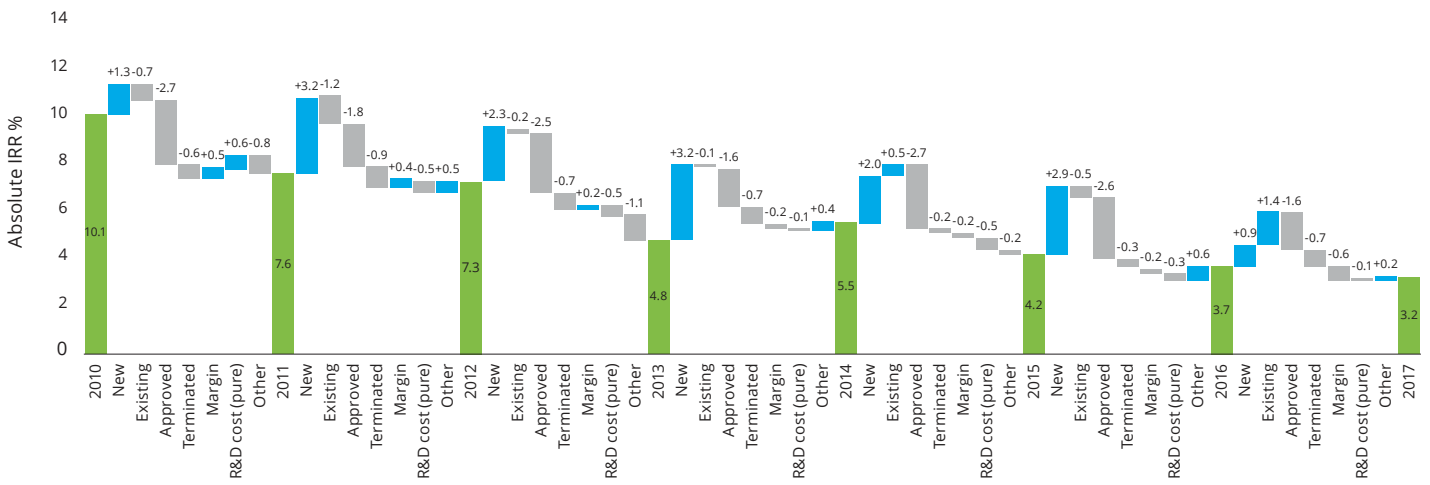
Source: Deloitte research, 2017

Figure 18. Three-year rolling average returns on late-stage portfolio, 2010-17
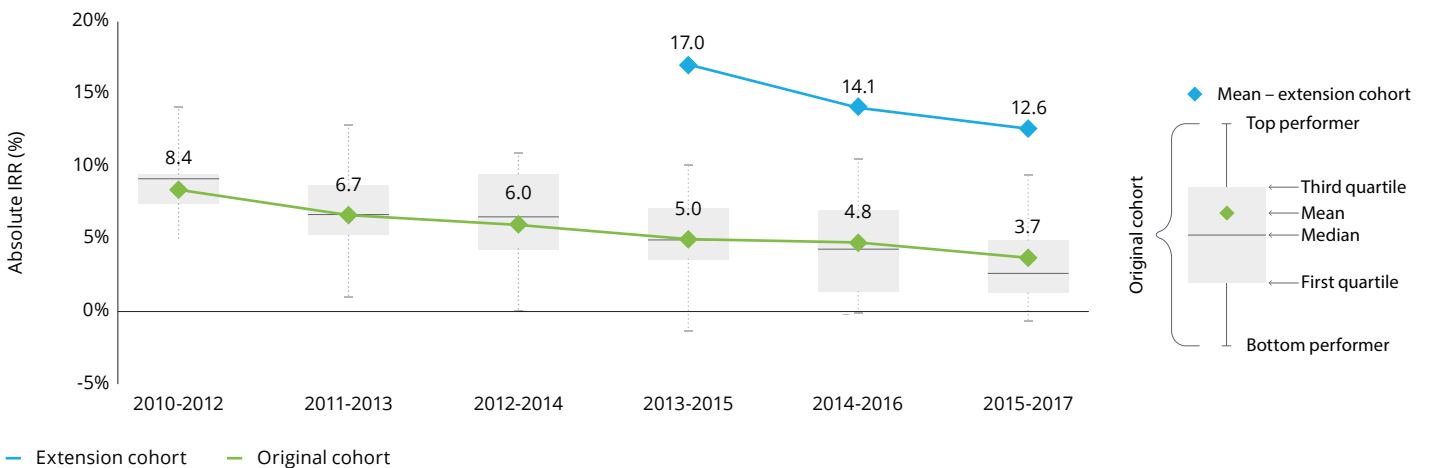
Source: Deloitte research, 2017

Figure 19. Three-year rolling average R&D cost to develop an asset from discovery to launch, 2010-17
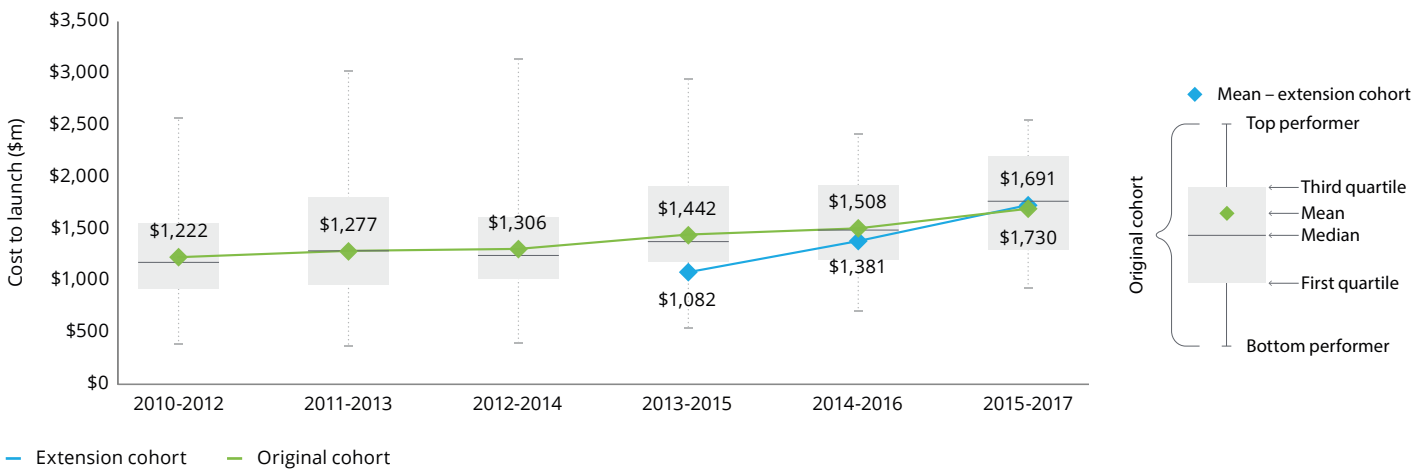
Source: Deloitte research, 2017

Figure 20. Three-year rolling average peak sales per late-stage pipeline asset, 2010-17
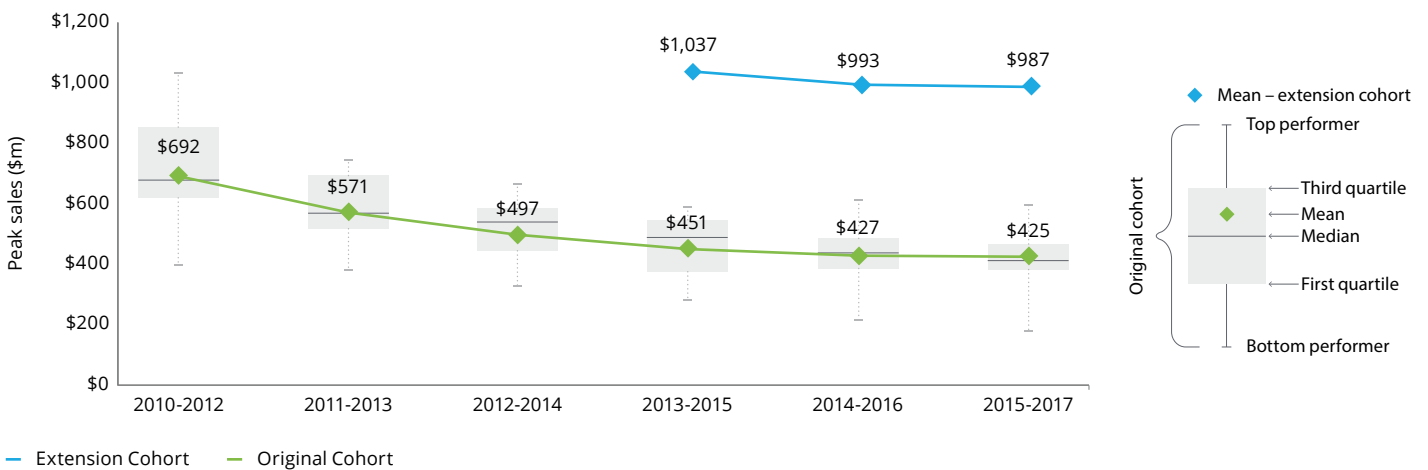
Source: Deloitte research, 2017

Contacts

Authors

Mark Steedman
Manager
UK Centre for Health Solutions
Deloitte LLP
+44 (0) 20 7007 8857
msteedman@deloitte.co.uk

Karen Taylor
Director
UK Centre for Health Solutions
Deloitte LLP
+44 (0) 20 7007 3680
kartaylor@deloitte.co.uk

Mark Stockbridge
Manager
Life Sciences R&D Advisory
Deloitte MCS Ltd
+44 (0) 20 7303 7539
mstockbridge@deloitte.co.uk

Casey Korba
Manager
US Center for Health Solutions
Deloitte Services LP
+1 (202) 748 1846
ckorba@deloitte.com

Sonal Shah
Senior Manager
US Center for Health Solutions
Deloitte Services LP
+1 (212) 653 6025
sonshah@deloitte.com

Matthew Thaxter
Research Analyst
UK Centre for Health Solutions
Deloitte LLP
+44 (0) 20 7007 7975
mthaxter@deloitte.co.uk

Deloitte EMEA contacts

Colin Terry
Partner
Life Sciences R&D Advisory
Deloitte MCS Ltd
+44 (0) 20 7007 0658
colterry@deloitte.co.uk

Julian Remnant
Partner, EMEA Life Sciences
R&D Advisory Lead
Deloitte MCS Ltd
+44 (0) 20 7303 3303
jremnant@deloitte.co.uk

Hanno Ronte
Partner
Life Science & Healthcare
Monitor Deloitte
+44 (0) 20 7007 2540
hronte@deloitte.co.uk

John Haughey
Partner, Life Sciences and Healthcare
Leader, UK & Switzerland
Deloitte MCS Ltd
+44 (0) 20 7303 7472
jhaughey@deloitte.co.uk

Mike Standing
Partner, Life Sciences and Healthcare
Leader, EMEA
Monitor Deloitte
+44 (0) 20 7007 3178
mstanding@deloitte.co.uk

Deloitte US contacts

Neil Lesser
Principal, Life Sciences R&D Practice Leader
Deloitte Consulting LLP
+1 (215) 446 4364
nlesser@deloitte.com

Daniel Ressler
Principal
Life Sciences R&D
Deloitte Consulting LLP
+1 (215) 299 5210
dressler@deloitte.com

Gregory Reh
Principal, Global Sector Leader
Life Sciences
Deloitte Consulting LLP
+1 (215) 997 7559
grreh@deloitte.com

GlobalData contacts

David Abramson
Global Director of Pharma Consulting
GlobalData
+44 (0) 20 7832 4343
david.abramson@globaldata.com

Bornadata (Bonnie) Bain, PhD
Global Head/EVP, Healthcare Operations
and Strategy
GlobalData
+1 (617) 747 4136
bonnie.bain@globaldata.com

Revati Tatake, PhD
Global Director of Databases and
Analytics, Healthcare
GlobalData
+1 (646) 395 5469
revati.tatake@globaldata.com

Contact information
To see more research and sign up for future publications visit:
www.deloitte.co.uk/centreforhealthsolutions

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