

Nurturing growth

Measuring the return from
pharmaceutical innovation 2021

Contents

Foreword	01
Infographic	02
Executive summary	04
Measuring the return from pharmaceutical innovation	06
The key drivers transforming the R&D paradigm	13
Methodology	22
Endnotes	25

Deloitte Centre *for*
Health Solutions

 **GlobalData.**

The Deloitte Centre for Health Solutions: Turning evidence into action

We are the research arm of Deloitte's Life Sciences and Health Care practices. The UK Centre's team of researchers, working in partnership with colleagues from the US Center for Health Solutions, aim to be a trusted source of relevant, timely and reliable insights on emerging trends, challenges and solutions. We combine creative thinking, robust research and our industry experience to develop evidence-based perspectives on some of the biggest and most challenging issues to help our clients to transform themselves and, importantly, benefit the patient.

At a pivotal and challenging time for the industry, we use our research to encourage collaboration across all stakeholders, from pharmaceuticals and medical innovation, health care management and reform, to the patient and health care consumer.

In this publication, references to Deloitte are references to Deloitte LLP, the UK affiliate of Deloitte NSE LLP, a member firm of Deloitte Touche Tohmatsu Limited.

GlobalData is a global data & insights solution provider who, for over 40 years, has been helping over 4,000 companies worldwide to make more timely, fact-based decisions. Our mission is to help our clients succeed and be more innovative by decoding the future and reducing the noise & uncertainties surrounding the world of today. We do this by providing market data, competitive insights and end-user perspectives which are delivered to our clients in an integrated way through a variety of different tools.

Foreword

Welcome to *Nurturing growth: Measuring the return from pharmaceutical innovation 2021*, the twelfth annual report from the Deloitte Centre for Health Solutions, exploring the performance of the biopharmaceutical industry (biopharma) and its ability to generate returns from its investment in innovative new products. During the past 22 months the world has navigated novel and constantly evolving threats, healthcare industries have adopted new ways of working while trying to protect people from harm, and society has suffered overwhelming loss and lasting changes to the way it measures, perceives and responds to risks. By early 2021 regulatory approval of the emergency use of several new treatments and vaccines, developed and manufactured in record time, provided a light at the end of the tunnel. We therefore examine, in addition to our traditional analysis of research and development (R&D) productivity, the impact of the pandemic on the pipelines of our cohort of leading biopharma companies.

Between 2010 and 2021 our *Measuring the return from innovation series* tracked the return on investment that an original cohort of 12 leading global biopharma companies might expect to achieve from their late-stage pipeline using the same comprehensive and consistent methodology. For the past eight years we also tracked the performance of an extension cohort of four more specialised biopharma companies (reduced to three in 2020 due to the merger of one extension company with an original company). Moreover, the systemic declining returns on investment meant the performances of the extension cohort and original cohort were converging. As a result, the 2020 report was a transition report that considered the performance of the two cohorts as a single combined cohort. This year's report again presents the results for the combined cohort.

Until 2020, the combined cohort had seen a decade-long decline in projected R&D productivity, reflecting the challenges faced by the industry more widely. However, in 2020, for the first time since 2014, the average internal rate of return (IRR) saw a small uptick, suggesting signs of a potential reversal in the declining trend. This year, our 2021 analysis shows a much larger improvement in the combined cohorts IRR with ten of the 15 companies all seeing an increase in their IRR. Even if we exclude COVID-19 related emergency-approval assets, the projected IRR in 2021 is still higher than the small uptick in our 2020 *Seeds of change* report.

Crucial drivers for this change have been a modest reduction in R&D cycle times and some companies seeing impressive improvements in peak sales projections. The average cost of developing a compound from discovery to launch has declined as the industry begins to capitalise on the development of some novel trial designs and improvements in efficiency through the digitalisation of drug discovery and development. There is no doubt that the COVID-19 pandemic has galvanised improvements with the 'need for speed' becoming all-encompassing and the unparalleled rate of approval of COVID-19 treatments and vaccines.

This year we have seen signs of progress, building on the 'seeds of change' we identified last year, due to faster drug development and higher valued pipelines. The collaborative stance with regulators and the scale and extent of partnership working across the health ecosystem has been a crucial enabler of vaccine development and has set a precedent for what the future could look like. Greater IRRs will spur further innovation benefitting patients, especially those who have no effective treatments, but only if the collaboration between organisations and regulators that emerged during the pandemic can become fully embedded and the use of digital and other transformative approaches to expedite drug development is nurtured and adopted at scale.



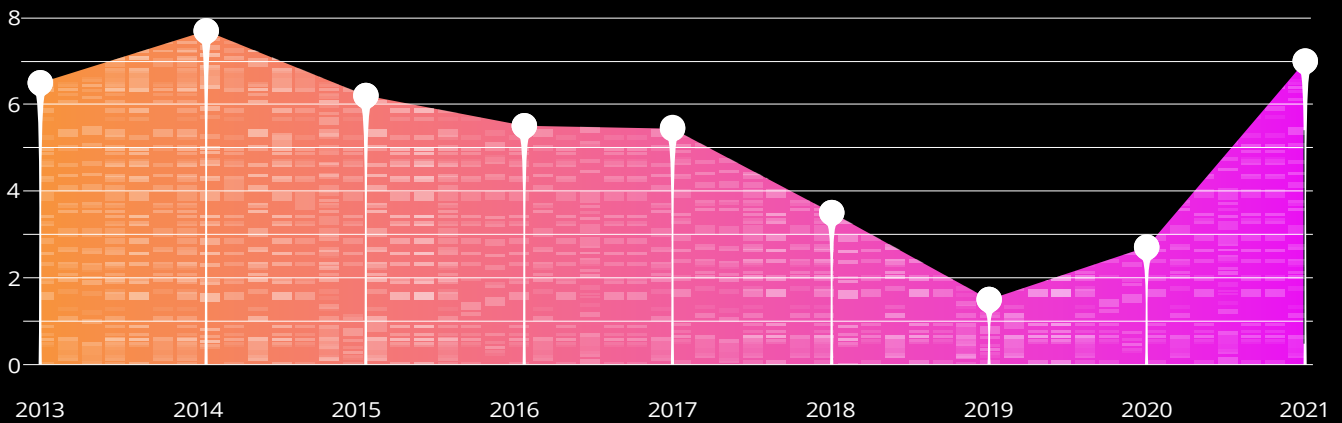
Colin Terry
Partner
EMEA Life Sciences R&D Leader



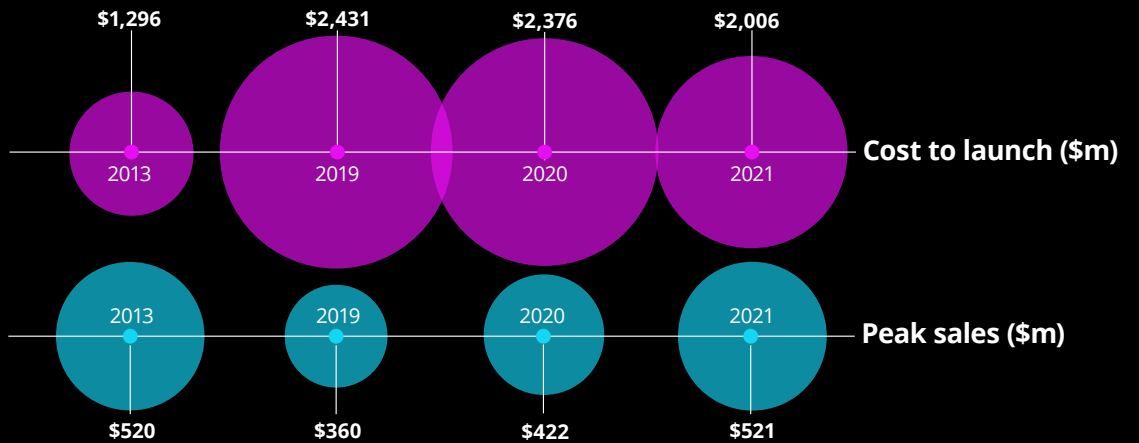
Neil Lesser
Principal
US Life Sciences R&D Leader

2021 results for our combined cohort of 15 biopharma companies

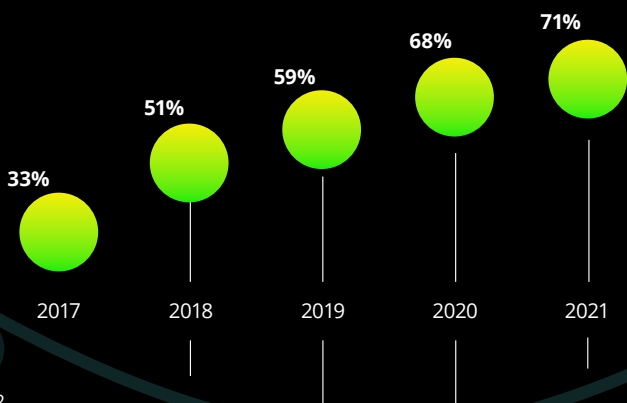
R&D returns have seen a large **uptick** in 2021
 IRR is the **highest** it has been **since 2014**



Cost to bring an asset to market has declined over the past three years at the same time as peak sales forecasts have **increased**



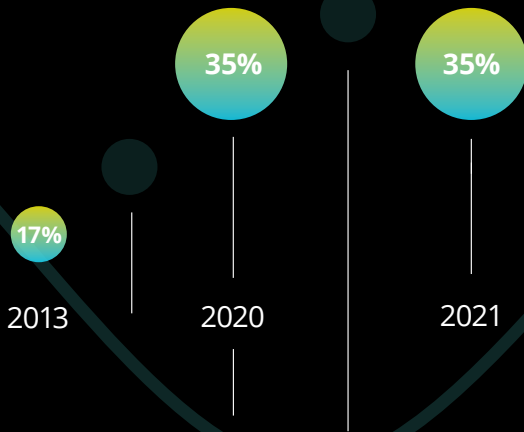
Companies are continuing to **increase proportion of external sources** of innovation



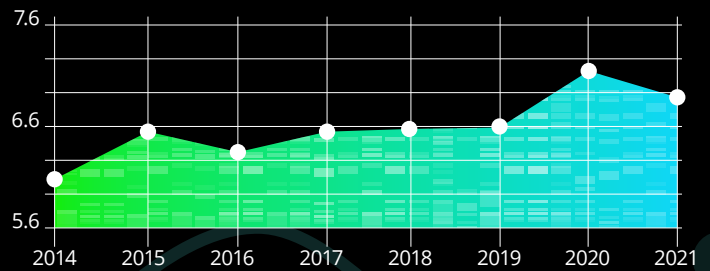
46%
 of late-stage assets are co-developed
 (up from 32% in 2020)

The proportion of the late stage pipeline focused on **infectious disease** assets has **grown by four percent since 2020**

Oncology pipeline share has **doubled** since 2013 and now stayed the same in both 2020 and 2021 with the largest share of the late-stage pipeline



Cycle times have **declined to 6.9 years** after climbing for four years



COVID-19 phase III **trials were 3.7 times faster** than non-COVID-19 infectious disease trials



Sustaining the momentum of change from COVID-19

Unlock the power of collaborative data sharing

Focus on streamlined protocol design

Increase patient centricity, health equity and trust

Integrate ESG initiatives into R&D

Build a digital talent pool

Expand use of digital technologies

Selectively pursue transformative development approaches

Strive for greater diversity in clinical trials

Enable at-risk development for high priority programmes

Executive summary

Advances in science and technology continue to drive improvements in care outcomes and fuel innovation across the biopharma industry. Our 2021 analysis shows a marked improvement in the average internal rate of return (IRR) on biopharma innovation for our combined cohort. While there is no doubt that a large part of this improvement is driven by COVID-19 related assets, particularly the increase in average peak sales forecasts, even if COVID-19 emergency-approval assets are excluded the slight uptick in IRR seen last year has risen further in 2021. Clinical cycle times have also reduced, after a seven-year high in 2020, albeit driven by the accelerated completion of trials for COVID-19 treatments and vaccines. Importantly, the pandemic has expedited the adoption of digital solutions, leaving the industry well-placed to reflect on the lessons learned and capitalise on process optimisation to fundamentally change the drug research and development paradigm.

Our series of reports on *Measuring the return from pharmaceutical innovation* analyse the return of investment that 12 large-cap biopharma companies (known as our original cohort) might expect to achieve from their late-stage pipelines and has provided insights into the state of biopharma R&D since 2010. Our analysis of this cohort between 2010 and 2014 indicated a steady decline in the average internal rate of return (IRR) with an inverse correlation between IRR and company size. In 2015, therefore, we added an extension cohort of four smaller, more specialised companies and retrospectively analysed their R&D investments back to 2013.

Over the subsequent six years, our analysis of the IRR of both cohorts showed a continuing decline. The performance of the two cohorts also converged as the extension cohort extended their therapy area focus and increased their investment in R&D to the extent that they became much closer in characteristics and performance to the original cohort. Furthermore, a company in the original cohort acquired a company in the extension cohort. Consequently, as explained in our 2020 report, *Seeds of*

change, we have now combined the original and extension cohorts to create a 'combined' cohort of 15 companies with performance data tracked back to 2013.

In 2020, we also expanded our analysis to measure the IRR of five further biopharma companies to give a more accurate picture of the overall industry. However, as we only have two data points for these additional five companies, we have continued to focus this year's report on the 15 companies in the combined cohort. Where relevant, we also draw on insights from the two years of analysis of the additional five companies.

Measuring the return from pharmaceutical innovation

Our measurement of the IRR is used as a proxy of R&D productivity and factors in the average cost to develop an asset in each company's pipeline and the average forecast sales from these assets once launched. Our 2021 analysis shows a large uptick in the projected IRR for the combined cohort to 7.0 per cent, from 2.7 per cent in 2020. Ten of the 15 companies have increased their projected IRR, albeit the range between the top and bottom performers in 2021 is much larger than

in 2020 (and is the largest range in performance since 2015).

Even if we exclude COVID-19 related assets with emergency approval, the projected IRR is 3.2 per cent which is still higher than the 2.7 per cent witnessed in our 2020 *Seeds of change* report.

The average cost to develop an asset, including the cost of failure, decreased in 2021 to \$2,006 million from \$2,376 million in 2020 (albeit this is still an increase compared to the \$1,296 million cost per asset in 2013). This decrease in average cost per asset between 2020 and 2021 is mainly due to the increase in the number of assets in the combined cohort's late-stage pipeline. In 2021, the combined cohort had a total number of 242 late-stage assets, an increase from 210 in 2020 (this is the largest number of assets in the late-stage pipelines of our combined cohort since 2013). The average is 16.1 assets per company, albeit there is wide variation across companies (from six to 26 assets).

The average forecast peak sales per pipeline asset has continued the upward climb seen in 2020, but this is driven

largely by the very high sales forecasts for COVID-19 assets and one high-value late-stage neurological asset.

Specifically, the average forecast peak sales per pipeline asset for the combined cohort increased from \$422 million in 2020 to \$521 million in 2021. Six of the 15 companies in the cohort improved their projected peak sales per asset compared to 2020. The range of forecast peak sales across companies in 2021 also increased, due to high sales forecasts for COVID-19 vaccines.

Sources of innovation are increasingly external

For the past four years, the combined cohort has relied on external sources of innovation for more than 50 per cent of the late-stage pipeline revenues, based on non-risk adjusted total inflows. The percentage increased from 51 per cent in 2018 to 71 per cent in 2021 (following year-on-year decreases from 52 per cent in 2013 to 33 per cent in 2017).

This increasing trend of sourcing assets through external innovation is indicative of pharma companies seeking to augment their innovation pipeline through collaborations and scientific partnerships with other, often smaller, players. It also reflects significant investment from venture funding and early-stage financing over recent years. Furthermore, the proportion of assets that have been co-developed increased from 32 per cent in 2020 to 46 per cent in 2021. This pattern is mirrored in the five new companies which we have started to analyse (in 2021, 82 per cent of their late-stage pipeline assets were from an external source, compared to 72 per cent in 2020).

Cycle times have dipped slightly

Since 2017 there has been a trend towards longer cycle times. However, in 2021 we have seen a slight improvement, to an average of 6.9 years, compared to the 2020 seven-year high of 7.14 years. This decrease in cycle times is driven by the expedited completion of studies for COVID-19 therapies and vaccines. However, the average cycle time is still above pre-pandemic levels of 6.64 years in 2019.

This reinforces the need to optimise processes and fundamentally change the drug development paradigm, as the 'need for speed' continues to be a vital factor for improving R&D productivity.

Infectious disease focus is growing

The proportion of the late-stage pipeline focused on infectious diseases has grown to 14 per cent in 2021, an increase of four percentage points compared to 2020, primarily due to the surge in the number of COVID-19 vaccines and other treatments under development. The pandemic has substantially raised the profile of vaccines as effective public health intervention tools and has also highlighted novel techniques such as mRNA technology, increasing the prospect of more effective and modifiable vaccines for other diseases.

Indeed, vaccines are expected to increase company revenues across modalities over the next few years as new vaccines to combat infectious disease, and other modalities including oncology, enter early-stage pipelines and the COVID-19 vaccination programmes expand across the developing world and include younger populations and booster dosing.

Lessons from the COVID-19 experience

Biopharma companies should expand the use of some of the more successful COVID-19 development measures to plan, design and execute studies more efficiently across their development portfolios. The learnings that companies could incorporate into their routine development operations include:

- enabling at-risk development for high-priority programmes by identifying programmes with a high probability of success and allowing them to bypass certain stage-gates to enable the seamless transition from one phase of development to the next
- expanding collaborative dialogue with regulators to accelerate the development of urgently needed therapies through data-sharing infrastructure and harmonising requirements across geographies

- focusing on streamlined trial protocol design with a limited number of relevant endpoints to reduce the burden on site staff, avoid protocol deviations and save development time
- pursuing transformative development approaches with master protocols and adaptive trial design to enable the rapid assessment of therapies
- accelerating the use of digital technologies to conduct hybrid studies, optimise site selection, recruit diverse study populations and capture data from and manage patients remotely
- striving for greater diversity in clinical trials to ensure study populations match the prevalence of disease across racial and ethnic groups.

Sustaining the momentum of change

To drive a more productive future for R&D, with more equitable and quicker access to new therapies, companies should nurture the growth identified in 2021 through:

- unlocking the power of collaborative data sharing to build on prior and emerging knowledge, reduce duplication of research efforts, and curate research-grade real-world data (RWD) with cloud-based capabilities across ecosystems
- building a digital talent pool to expand the use of data science driven and hybrid study approaches by rethinking talent strategies, creating alliances to access digital talent at source, and investment in reskilling existing talent
- improving health equity and building trust through a focus on patient centricity globally, including wider application of access and affordability programmes and demonstrating humanity, transparency, capability, and reliability
- integrating environmental, social and governance (ESG) initiatives into R&D by not only considering the sustainability of clinical trial footprints and supply chains but also meeting society's expectations about equity of access to experimental and approved therapies

Measuring the return from pharmaceutical innovation

Our annual *Measuring the return from pharmaceutical innovation* report series analyses the projected return on investment that biopharma companies can expect to earn from their late-stage pipelines. In this twelfth report of the series, our results are inevitably influenced by industry's prodigious response to the COVID-19 pandemic, especially the rapid development and manufacture of several successful treatments and vaccines. Indeed, our 2021 results show a notable uptick in the average return for our cohort of 15 R&D companies, with ten of the cohort enjoying individual upticks in R&D returns. This suggests that the small improvements we saw last year, in our *Seeds of change* report, have been nurtured with the adoption of innovative approaches to R&D leading to shorter cycle times, increases in projected revenues and a reversal of the decline in returns that the cohort experienced between 2013 and 2019.

About this report

In 2010, our inaugural annual report on *Measuring the return from pharmaceutical innovation* provided unique insights into the internal rate of return (IRR) on investment that 12 large-cap biopharma companies might expect to achieve from their late-stage pipelines. In 2015, we expanded our analysis to include an extension cohort of four more specialised companies, retrospectively calculating their IRR back to 2013. Over the subsequent six years the expected returns of the original cohort fell year-on-year. At the same time, the much higher returns experienced initially by the extension cohort fell more dramatically, leading to a convergence in the performance of the original and extension cohorts (see our 2019 *Ten years on report*).¹ Moreover, with the acquisition of one of the extension cohort companies by one of our original cohort companies in 2020, our extension cohort was reduced to three companies. Therefore, in our 2020 analysis, we merged the original and extension cohorts to create a 'combined cohort' of 15 companies.²

In 2020, we also expanded our analysis to include five new companies to start measuring the IRR of the top 20 biopharma companies by R&D spend. This aims to provide a more balanced picture of the overall industry. However, as we only have two years' worth of data for the additional five companies, this year we are still focusing on the IRR trend data for the combined cohort of 15 companies.

The trend data for the combined cohort starts in 2013, the first year in which we calculated the IRR for the extension cohort. Where relevant we draw on insights from our two years of analysis of the performance of the additional five R&D companies. Our intention is that next year's analysis will include these additional companies in a new cohort of 20 companies.

Methodology used to measure the return from pharmaceutical innovation

While the composition of the cohort may have changed, we have continued to apply the same consistent and objective methodology which focuses on each

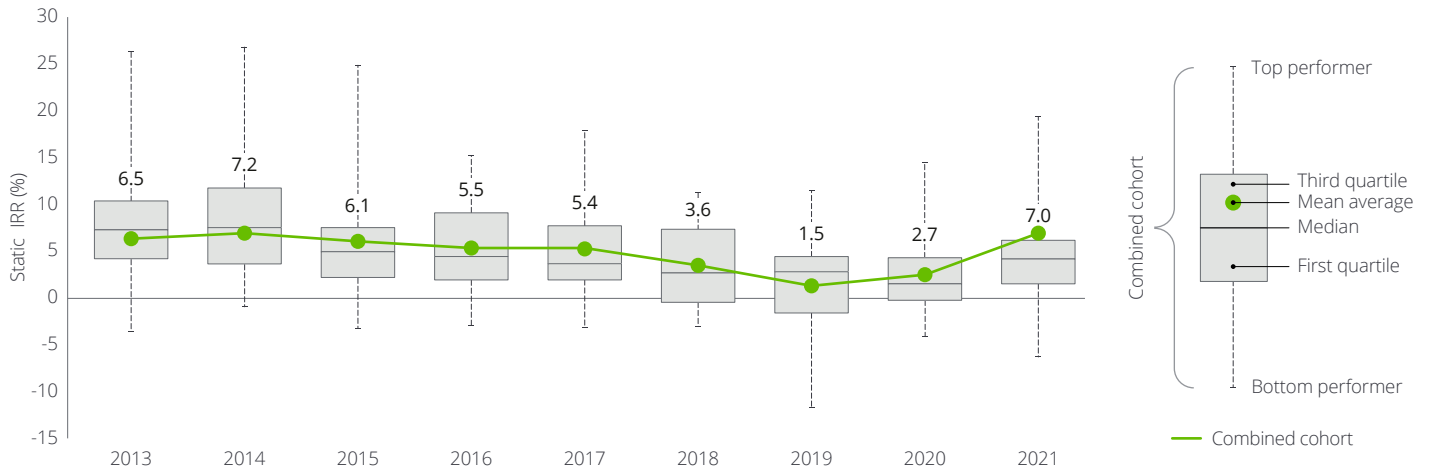
company's late-stage pipeline (assets that are filed, in Phase III or Phase II with breakthrough therapy designation, as at 30th April each year). Assets with emergency use approval like the vaccines are considered to still be part of the late stage pipeline as are the costs of developing these assets.

We use two inputs to calculate the IRR:

- the total R&D expenditure incurred by a company in bringing their assets to launch (based on publicly available information from audited annual reports and readily available data from third-party data providers)
- a forecast estimate of the future revenue that these assets could expect to earn following launch.

As assets are approved, forecast revenues move from the late-stage pipeline into the commercial portfolio, moving out of scope of our analysis and decreasing the value of the late-stage pipeline under review.

Figure 1. Return on late-stage pipeline, 2013-21 – combined cohort



Source: Deloitte LLP, 2021

Our analysis also accounts for multiple factors such as forecast revenue splits where a particular asset is in development for multiple indications; the impact of in-licencing and mergers and acquisitions (M&A) on R&D costs; success rates in late-stage development and the impact of clinical cycle times.

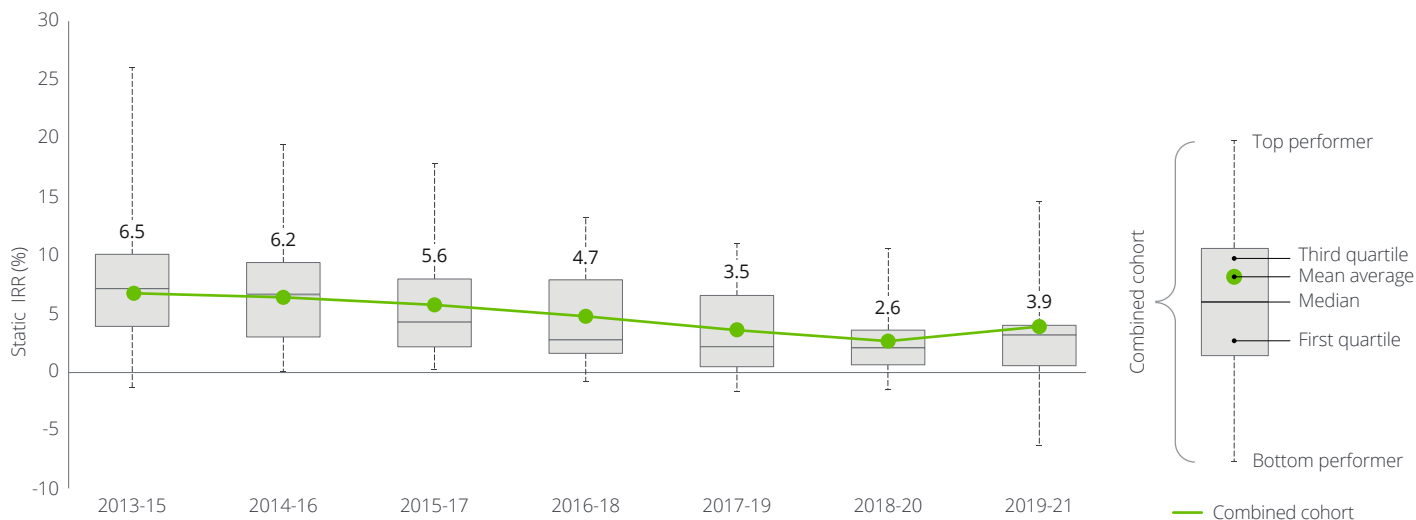
This year, as we did last year, we have a separate analysis of the impact of the pandemic on clinical trials. As we are continually working to improve the methodology and modelling underpinning this analysis, some numbers have been re-stated. The methodology appendix provides more detail.

Projected returns from innovation have continue the upward trend

Last year, we saw ‘seeds of change’ following six years of decline, albeit it was only a slight uptick (from 1.5 per cent in 2019 to 2.7 per cent in 2020). This trend has continued this year, with the combined cohort experiencing a much larger uptick to 7.0 percentage points, from 2020 to 2021. Figure 1 shows the overall trend line for IRR between 2013 and 2021 for the combined cohort indicating that the average IRR has returned to a value similar to that last seen in 2014. Even if we exclude COVID-19 related assets with emergency approval, the projected IRR is 3.2 which is still higher than the small uptick of 1.7 per cent witnessed in our 2020 *Seeds of change* report.

The top two performing companies in our combined cohort achieved forecast returns greater than 18 per cent, with 13 out of the 15 companies achieving positive returns; and ten of the 15 companies improving their average forecast IRR in 2021 compared to 2020. The steep increase in the forecast average IRR this year is mainly due to COVID-19 related assets including vaccines and treatments and positive trial data for one high-value late-stage neurological asset (albeit sales of the latter have underperformed following launch). A notable feature of these high-performing assets is that the medicines are intended to help large numbers of the population. Of our five additional companies analysed for the second year running, four improved their average forecast IRR compared to 2020, with three achieving positive returns.

Figure 2. Three-year rolling average returns on late-stage portfolio, 2013-21 - combined cohort



Source: Deloitte LLP, 2021

In 2020 we saw the narrowest range in performance between the top and bottom performer at 18.6 percentage points (top performer +14.6 per cent, bottom performer -4.0 per cent). In 2021 the range has increased to 25.9 percentage points (top performer +19.7 per cent, bottom performer -6.2 per cent). However, the range in 2021 is still less than the range in 2013 which was a 29.9 percentage points gap (top performer +26.6 per cent, bottom performer -3.3 per cent).

On a three-year rolling average basis, the average forecast IRR has increased to 3.9 for 2019-21, up from 2.6 in 2018-20, the first uptick seen in our three-year rolling average analysis (see Figure 2).

Drivers of change

Figure 3 presents the aggregate drivers of change for the combined cohort between 2013 and 2021. As we have seen every year in our *Measuring the return from pharmaceutical innovation* series, companies continue to innovate by investing in new assets, with the overall effect of this investment being a growth in IRR of 19 percentage points for the combined cohort of companies.

However, the rate at which companies have been replenishing their late-stage pipeline value has not previously been enough to counteract the successful approval and flow of value into the commercial pipeline, with an overall effect of -19.8 percentage points since 2013.

Figure 4 presents the aggregate drivers of change for the combined cohort between 2020 and 2021, demonstrating the impact existing assets have had on the improved IRR. The combined cohort have seen an increase of 4.4 percentage points in the value of projected returns from existing late-stage pipeline assets between 2019 and 2020. This is the highest year-on-year increase due to existing assets since our analysis began in 2010 (Appendix 2). This increase in forecast revenues from existing assets was driven largely by positive trial data for high-value assets and COVID-19 related vaccines and treatments.

A small increase in the number of approved assets

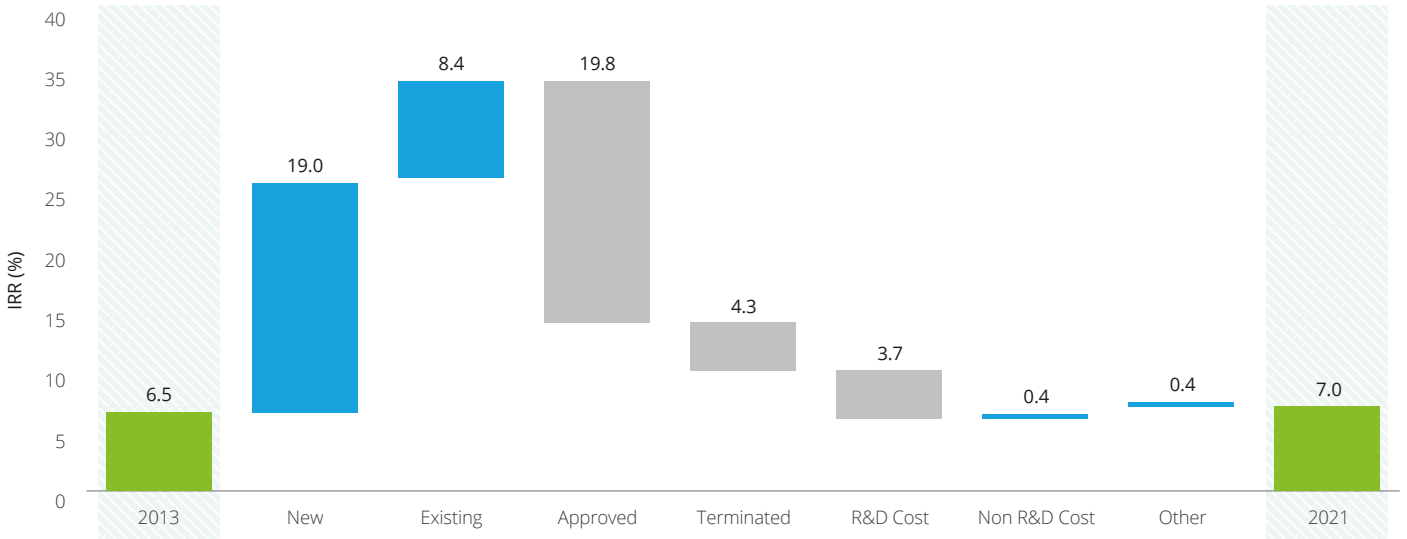
From 1 May 2020 to 30 April 2021, the combined cohort had a total of 54 assets approved, one more than the 53 assets in 2020.

These approved assets have forecast total sales of \$260 billion. This represents a 1.7 percentage point decline in projected returns between 2020 and 2021 (Figure 4).

Over the period 2013 to 2021 the decline in projected returns from approvals is 19.8 percentage points (Figure 3), demonstrating the importance of replenishing the pipeline compared to 2020. In 2021, terminations resulted in a 0.2 percentage point decline in IRR for the combined cohort (Figure 4). Since 2013, the overall effect of terminations has been a fall in IRR of 4.3 percentage points for the combined cohort (Figure 3) demonstrating the inherently risky nature of late-stage R&D.

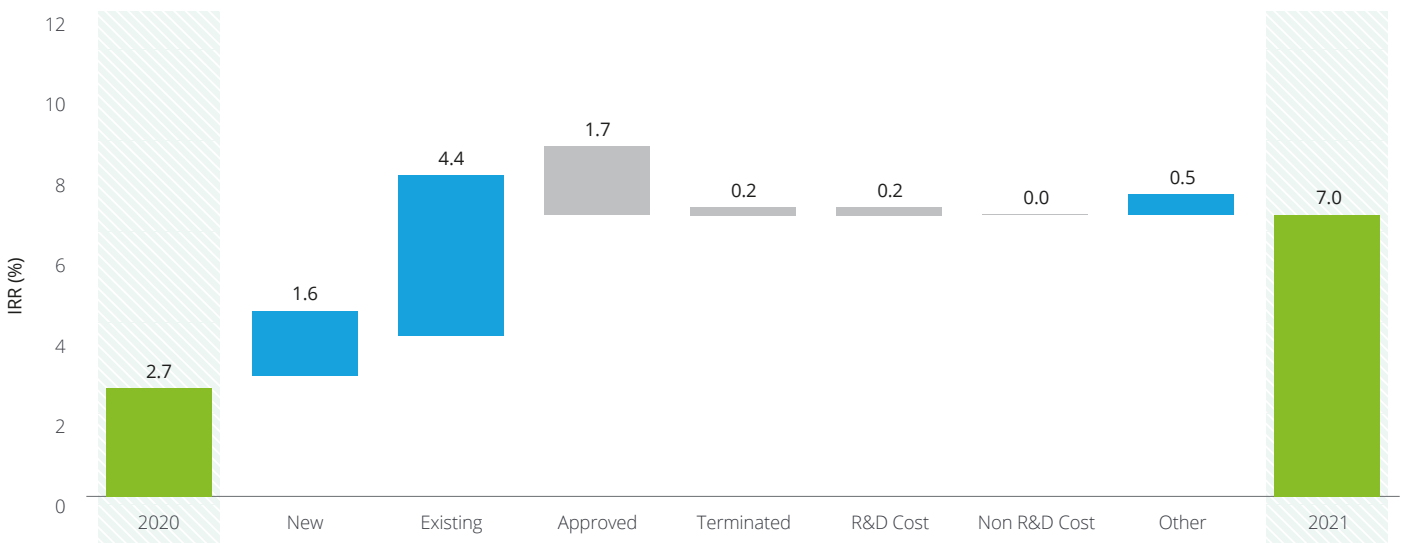
In 2021, there was an increase in IRR of 1.6 percentage points, due to 63 new assets entering the combined cohorts pipeline compared to 45 new assets that entered the pipeline in 2020. These new assets have forecast lifetime sales of \$278 billion.

Figure 3. Drivers of change in IRR, 2013-21 - combined cohort



Source: Deloitte LLP, 2021

Figure 4. Drivers of change in IRR, 2020-21 - combined cohort



Source: Deloitte LLP, 2021

The average number of assets in development has increased for the combined cohort

The combined cohort have a total of 242 late-stage assets, an increase from 210 in 2020. This increases their average number of assets to 16.1, the highest number of average late-stage assets seen since our analysis began for this cohort in 2013. As in all previous analysis, there is a substantial variation across the companies, from six to 26 assets as shown in Figure 5.

The average cost to develop an asset has decreased

In 2021, the combined cohort spent a total of \$126.9 billion on R&D, corresponding

to an increase of 31 per cent in underlying R&D expenditure compared to 2020. This figure increases to a total spend of \$141 billion if the additional five companies that we are in the process of integrating into the combined are included, an increase of 28 per cent in R&D expenditure compared to 2020.

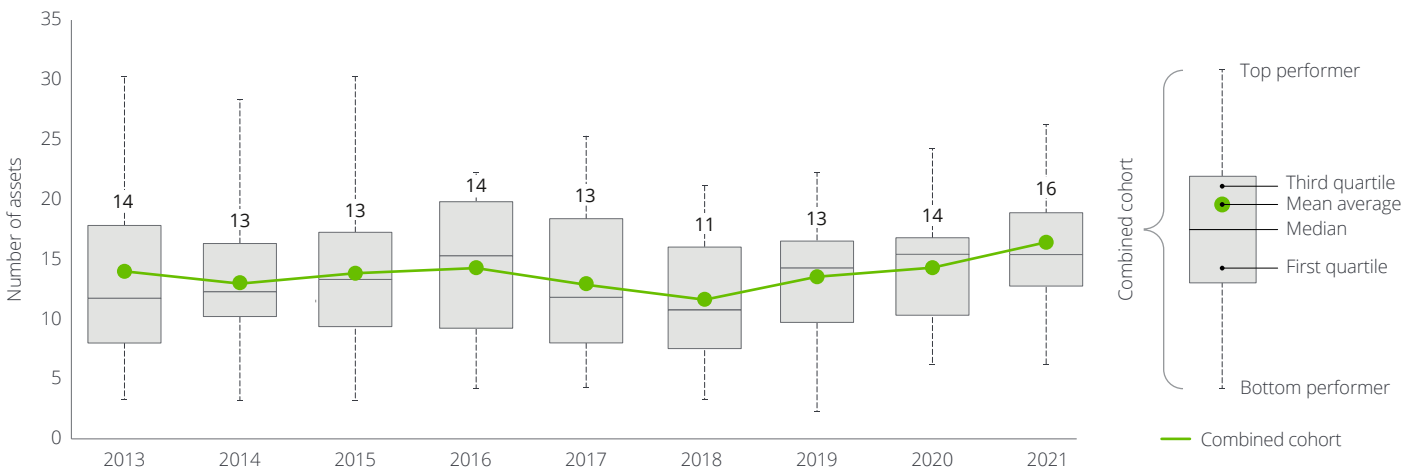
Figure 6 shows that the combined cohort's average cost to develop an asset was \$2,006 million, a decrease of \$370 million from 2020 (but nevertheless an increase of \$710 million from 2013). This decrease in 2021 compared to 2020 is due mainly to the overall increase in the number of assets in the late-stage pipeline.

The distribution of costs to develop an asset across the combined cohort has decreased slightly compared to 2020, from a range of \$4,621 million (highest cost: \$5,496 million, lowest cost: \$875 million) to \$4,192 million (highest cost: \$5,034 million, lowest cost \$842 million).

Average forecast peak sales continue the slight upward climb started in 2020

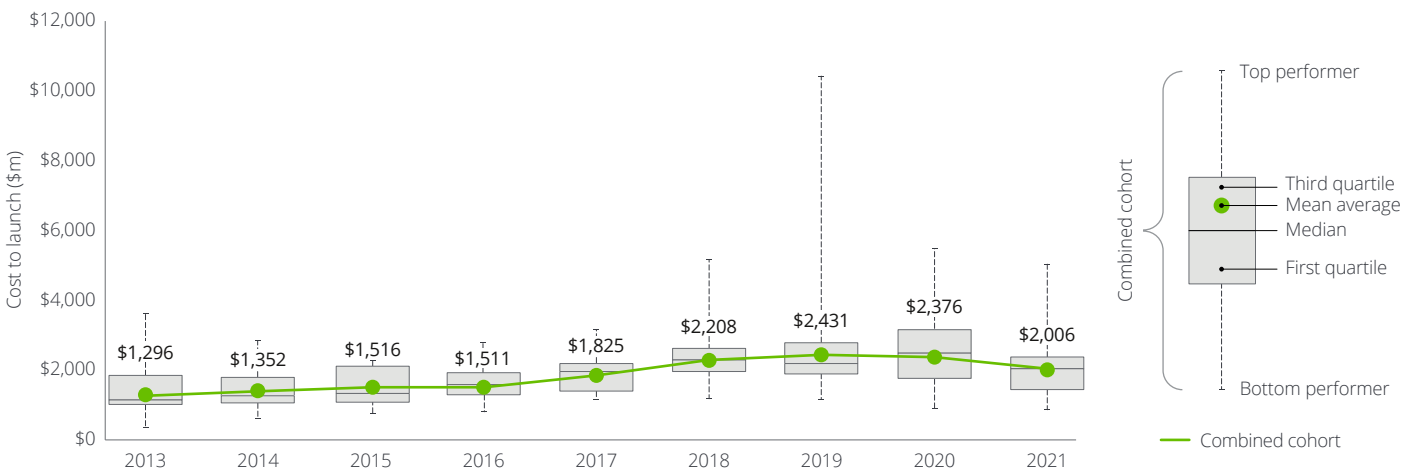
For the combined cohort, three companies achieved a forecast peak sales per asset greater than \$500 million in 2021, with six companies improving their projected peak sales per asset compared to 2020.

Figure 5. Average number of assets in late-stage pipeline, 2013-21 – combined cohort



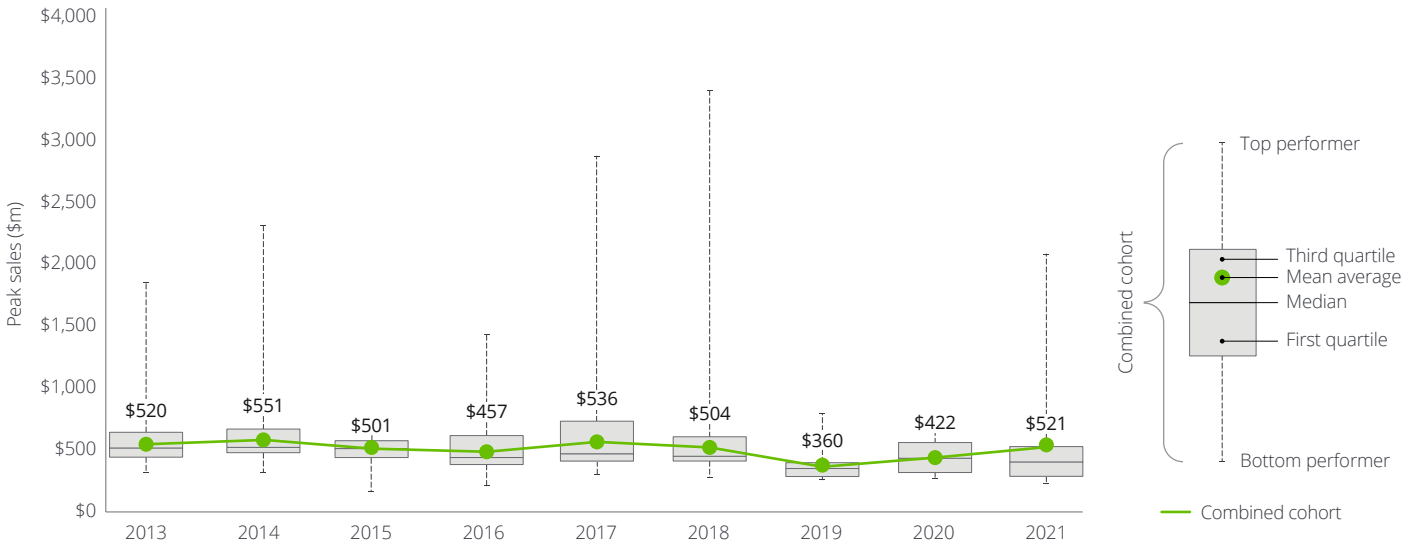
Source: Deloitte LLP, 2021

Figure 6. Average R&D cost to develop a compound from discovery to launch, 2013-21 – combined cohort



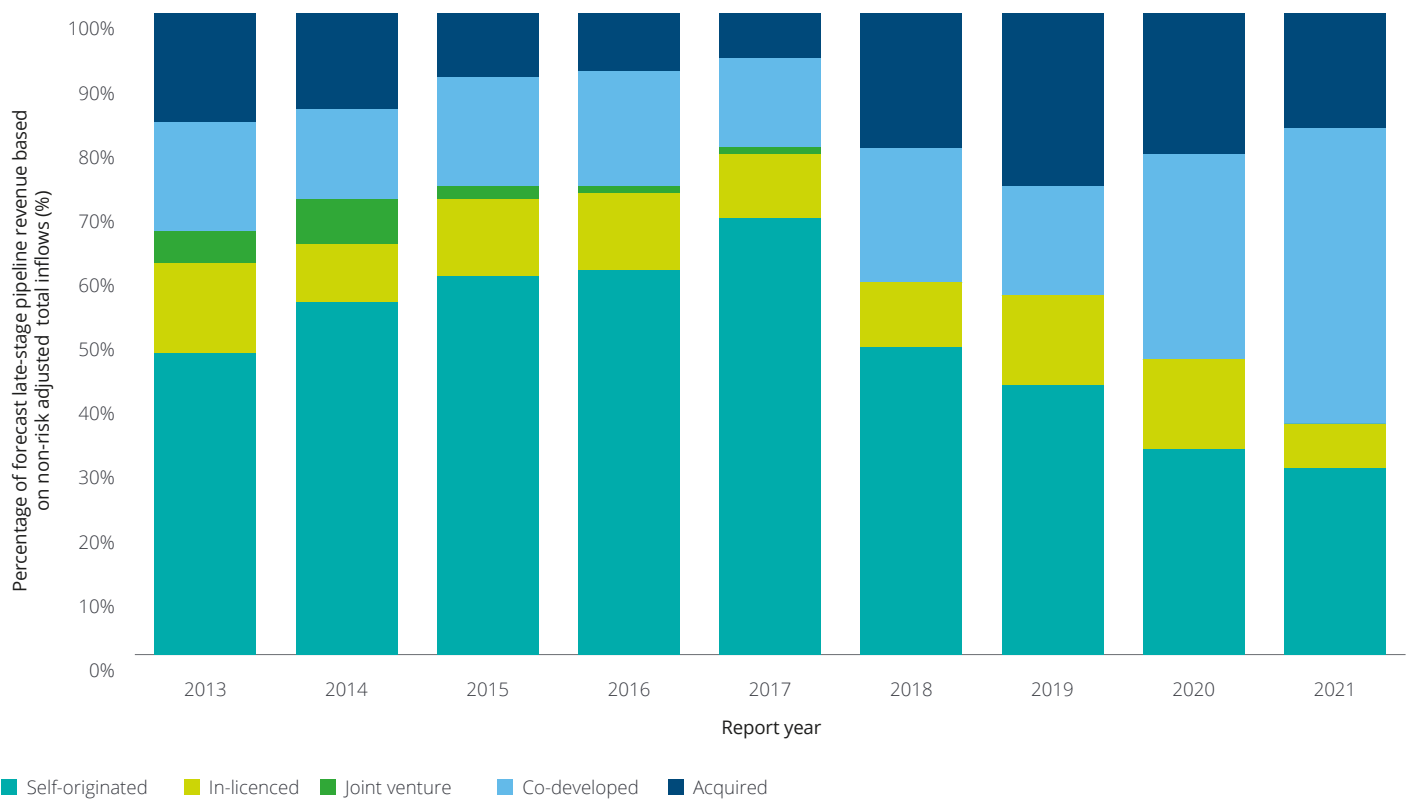
Source: Deloitte LLP, 2021

Figure 7. Average forecast peak sales per pipeline asset, 2013-21 – combined cohort



Source: Deloitte LLP, 2021

Figure 8. Proportion of late-stage pipeline sourced from internal and external sources, 2013-21 – combined cohort



Source: Deloitte LLP, 2021.

In 2021, average forecast peak sales per pipeline asset for the combined cohort increased from \$422 million in 2020 to \$521 million in 2021 as shown in Figure 7. The increase in the range of forecast sales, from \$481 million in 2020 to \$1,861 million in 2021, is mainly due to the high sales forecast for COVID-19 vaccines and a prospective neurological drug. If COVID-19 assets are excluded, the average peak sales forecasts declined from \$422 million to \$355 million.

The effect of COVID-19 assets on the combined cohort's pipeline

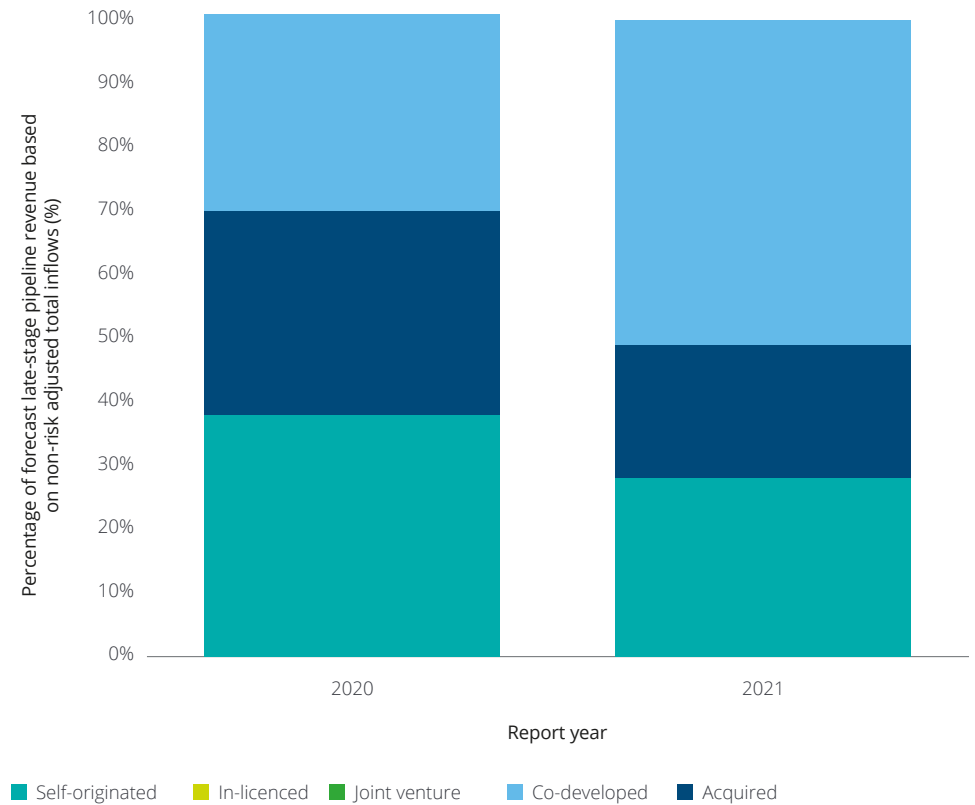
The pipeline of the combined cohort includes five COVID-19 related assets, with emergency use approval. Unsurprisingly, these had a significant impact on the 2021 analysis due to the expedited completion of trials as well as the unprecedented global need for these assets, leading to very high sales forecasts. Nevertheless, when these emergency approved COVID-19 assets are removed from the late-stage pipeline, the combined cohort still sees an uptick in IRR from 2.7 in 2020 to 3.2 in 2021 (see Appendix 2).

The average number of assets also remain at 16 per company (16.1 with the assets included to 15.8 without) and the large variation in asset numbers across companies also remains. However, the largest impact of removing the COVID-19 assets from the late-stage pipeline is on the average peak sale forecast per asset, which declines from \$422 million per asset in 2020 to an average peak sales forecast of \$355 million in 2021 (a decline of \$166 million).

The sources of innovation are increasingly external

Continuing the trend that we've seen for the past few years, since 2018, the sources of innovation for the late-stage pipeline of our combined cohort are increasingly external (see Figure 8).

Figure 9. Proportion of late-stage pipeline sourced from internal and external sources, 2020-21 – additional five companies



Source: Deloitte LLP, 2021.

This trend could be a result of the huge capital investment from venture and early-stage financing resulting in more external innovation being insourced as these assets get closer to commercialisation.

Notably this year has seen an increase in co-developed assets, with the forecast revenue from co-developed assets increasing from 32 per cent in 2020 to 46 per cent in 2021. This suggests that almost half of forecast revenues from the late-stage pipeline are being generated through collaborations and scientific partnerships.

A preview of the performance of the five additional companies in 2020 and 2021 shows that their trend largely mirrors that of the combined cohort.

Figure 9 shows how the proportion of forecast revenue from assets sourced externally by the five new companies has increased from 62 per cent of the late-stage pipeline in 2020, to 72 per cent in 2021. Furthermore, the largest growth is also an increase in forecast revenue from co-developed assets, which increased from 31 per cent in 2020 to 51 per cent of the late-stage pipeline in 2021.

The key drivers transforming the R&D paradigm

A crucial driver of IRR is clinical cycle time, which improved slightly in 2021 after a seven-year high in 2020. This was driven by the expedited completion of COVID-19 therapies and vaccine trials. Indeed, the lessons from the COVID-19 pandemic are beginning to transform the general approach to drug development. For example, the adoption of digital solutions has been accelerated, there is an increase in the risk appetite for high priority programmes and collaborative dialogue with regulators has expanded. We have also seen a growth in adoption of adaptive trial designs and more focus on ensuring greater diversity in clinical trials, both geographically and demographically. Moreover, COVID-19 has broadened the cohorts focus on infectious diseases. As a result, the industry is well-positioned to build on the momentum and the lessons learned to optimise processes and fundamentally change the drug research and development paradigm.

Cycle time for the combined cohort has improved slightly but remains above pre-pandemic levels

Over the past few years, increases in cycle times have presented a challenge to biopharma R&D productivity. The increases have been driven by the growing complexity of study protocols, a focus on developing more targeted and complex therapies, and difficulty in attracting and retaining trial participants. The disruptions to clinical trial activity particularly in the early months of the pandemic added to this, with development cycle times for the combined cohort spiking in 2020.

During our 2021 analysis, disruptions to routine drug development activity due to COVID-19 steadily declined.³ Analysis by GlobalData, across the industry, found that the number of trials impacted by COVID-19 declined from 1,210 between March and mid-November 2020 to less than 100 between mid-November 2020 and end of April 2021.

The development cycle time for our combined cohort has seen an improvement in 2021 (see Figure 10), owing to a decline in overall cycle time for Phase III studies. This decline is linked primarily to expedited completion of Phase III studies for COVID-19 therapies and vaccines. Our analysis suggests these studies were 3.7 times faster than non-COVID-19 infectious disease trials, owing to shorter enrolment time and use of digital technologies to accelerate study execution. Nevertheless, despite the dip, the overall cycle time for combined cohort continues to remain above 2019 levels, reinforcing the need to optimise processes or fundamentally change the drug development paradigm.

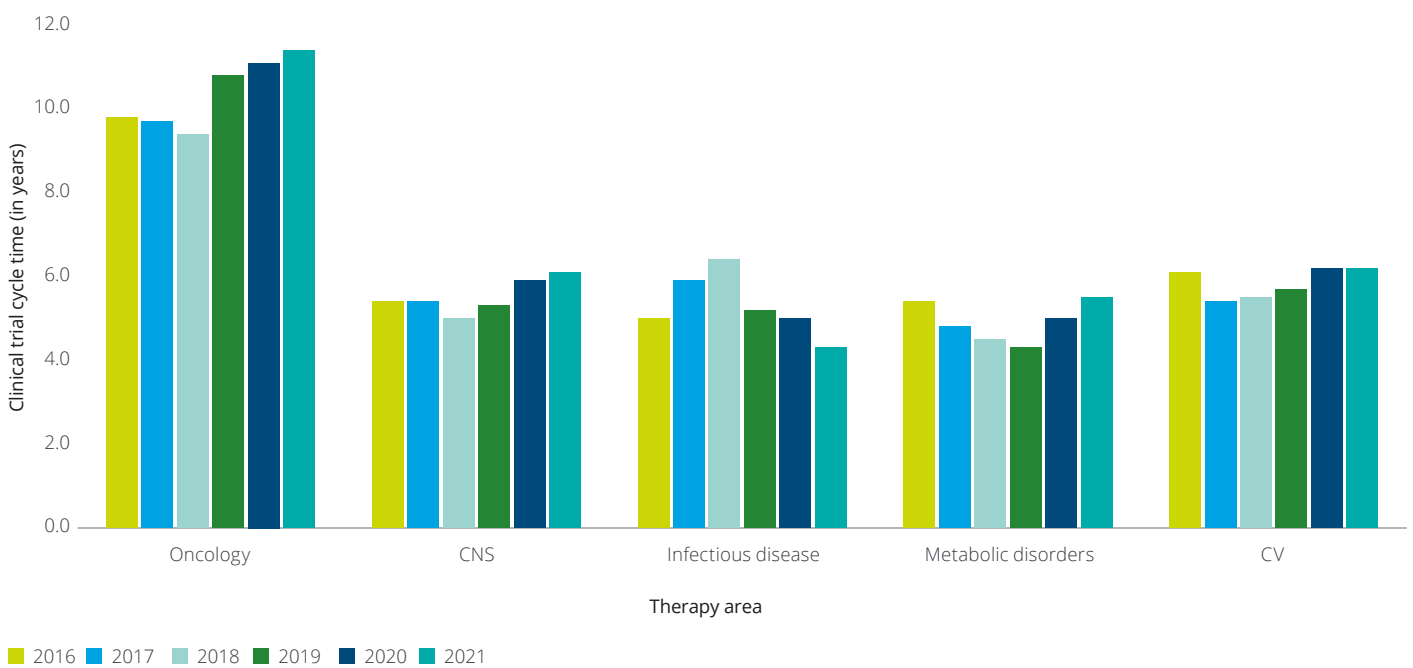
Incorporating lessons from the biopharma's COVID-19 experience into routine drug development

As highlighted in our 2020 report, and acknowledged widely, the unparalleled stakeholder collaboration, significant public and private funding, and regulatory flexibility enabled companies to bring multiple COVID-19 vaccines and therapies to market within unparalleled time frames.⁴ While the pandemic created the 'perfect storm' to achieve this extraordinary feat, there are several lessons from the COVID-19 drug and vaccine development approach that companies should consider incorporating into routine drug development operations.⁵ In particular, biopharma companies should evaluate and adopt the more effective COVID-19 development approaches and plan, design, and execute studies more efficiently in other therapy areas (TAs) and across their development portfolios (see Figure 11).

Figure 10. Average clinical trial cycle time and cycle time across TAs (in years)

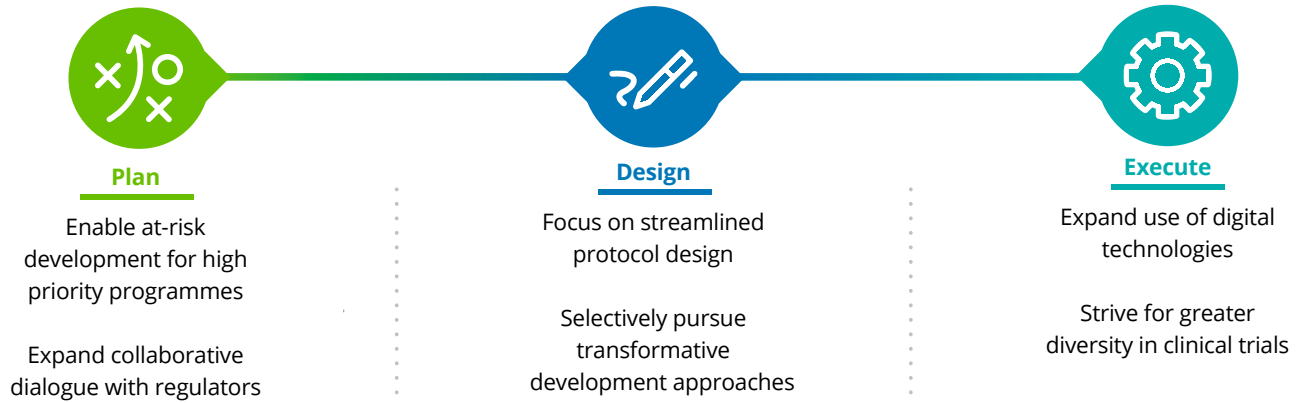


Note: Figures indicate time between start of Phase I trial to completion of Phase III trial



Source: Deloitte LLP, 2021

Figure 11. Incorporate the lessons from the R&D approaches adopted for COVID-19 into routine clinical development



Source: Deloitte LLP, 2021



Enable at-risk development for high priority programmes

In the race to address the humanitarian need created by COVID-19, companies ran R&D phases and activities in parallel to accelerate vaccine and therapy development. An unprecedented amount of funding enabled companies to deploy capital boldly and at risk by potentially absorbing the full financial risks of R&D.^{6,7}

Furthermore, the scale of unmet need challenged the orthodoxy of sequentially staging clinical trials to answer scientific questions and de-risk investments, before cautiously progressing to larger studies. For example, Pfizer adopted a combined Phase I/II trial to simultaneously assess safety, efficacy and dose levels of its vaccine candidate(s) and then ran a large Phase III trial, compressing development time to around nine months.⁸

Manufacturers also invested at risk to scale production capabilities, acquire raw materials, and begin mass producing vaccines, before pivotal studies were completed.

Biopharma companies should reconsider the governance processes needed post-pandemic to enable at-risk development for other high priority programs.

This involves identifying programmes with a high probability of success to enable study teams to bypass certain stage-gates and seamlessly transition from one phase of development to the next. Companies would also need to allocate additional resources to such programmes to invest in at-risk activities such as planning for pivotal trials in advance and accelerate study start-up activities (see case study 1).⁹

This should include using simulation and other tools to enable study teams to visualise the sequence of activities across global clinical operations, to identify areas or processes to carry out in parallel and to consider how and

where compressing timelines might be beneficial.

Expand collaborative dialogue with regulators

The expedited development of safe and effective COVID-19 vaccines and therapies required increased regulatory flexibility and active dialogue between the industry and regulators. This included regulators being open to adaptive trial designs, use of rolling data submissions while expediting protocol reviews, and providing real time scientific advice to companies.¹²

CASE STUDY 1

Expediting study start-up to test the world's first oral COVID-19 therapy

To accelerate Phase I trials of its oral antiviral drug for COVID-19, Merck undertook several study start-up activities in parallel. The company simultaneously submitted clinical trial applications in the US and UK and actively coordinated with regulators for review and approval of clinical trial applications and study protocols within 16 days. Additionally, pharmacy set-up activities which normally require two to three months to perform were completed within two weeks from project initiation. The study recruitment team also began pre-screening volunteers even before clinical trial applications were approved. Such parallelisation of study activities enabled the first patient to be dosed on day 23 that would have taken more than four months as per standard industry timelines.^{10,11}

There is now an opportunity for the industry to work with regulators to adapt some of the pandemic era regulatory flexibility to accelerate development of urgently needed therapies. For life threatening and debilitating conditions, companies could engage with regulators to actively accelerate protocol review, use rolling data submissions and even design minimalistic dossiers focused on safety and efficacy for approvals. This could lead to a new paradigm of regulators working hand in hand with industry rather than undertaking the current end of trial review discussion to expedite patient access to urgently needed therapies.¹³

“The agency’s approach to coronavirus therapeutics and vaccines should translate post-pandemic to some urgently needed products. Even if it is a partial application, particularly about a product that is urgently needed, we should be able to do rolling reviews so that we can expedite the process”

-Stephen Hahn, Ex-FDA Commissioner¹⁴

“Rolling reviews, were used very effectively, particularly in the context of vaccines. As normality resumes there will still be a place for them, although the extent to which they will be used needs to be discussed.”

- Emer Cooke, Executive Director European Medicines Agency¹⁵

Today, launching a drug across multiple geographies requires data to be submitted in various formats to meet the requirements of numerous regulatory agencies. This challenge has persisted for years, but there is cause for optimism with the launch of Accumulus Synergy in 2020. Accumulus is a non-profit organisation, established by ten of the industry’s leading biopharmaceutical companies, focused on developing a global information exchange platform to transform how drug innovators and health regulators exchange information and data.¹⁶ Having driven an unprecedented degree of collaboration across sponsors and international regulators and Accumulus is planning to deploy an initial technology release in 2021.¹⁷ Such initiatives could enable a future where regulatory practices are globally aligned, digitally driven, and regulatory agencies actively collaborate to share data and insights for the rapid assessment of new therapies.¹⁸



Focus on streamlined protocol design

Streamlining protocol designs to focus on a limited number of relevant endpoints enabled biopharma companies and academic institutions to determine the safety and efficacy of repurposed drugs and new therapies for COVID-19 at an unprecedented pace. One such example is RECOVERY, a master protocol trial led by the University of Oxford, UK, that has recruited over 45,000 participants and evaluated nine treatments so far, and continues to investigate others.¹⁹ The trial protocol involved capturing the most relevant patient outcomes (death, discharge, and need for ventilation), inputting key patient data into a simple online form, and mandating only one follow up assessment, reducing the load on already stressed NHS staff.^{20,21}

The RECOVERY model is now being implemented in sites in Asia and Africa to help build capacity and to find treatments that are suitable for different populations and healthcare settings.²²

Over the past decade, oncology trial protocols have grown in complexity to capture a high volume of secondary and exploratory endpoint data.^{23,24}

If applied to oncology, streamlined protocol design could reduce the burden on patients and site staff to understand and execute study processes, avoid protocol deviations, and save development time. This could also reduce the need for participants to undertake multiple site visits, procedures, and assessments, improving study retention rates.

Some companies are already encouraging study teams to create protocols that incorporate the most meaningful endpoints, eligibility criteria, and procedures. GlaxoSmithKline (GSK), for instance, has setup a protocol design lab to assess historical trial data (site recruitment data) and real-world data (disease prevalence, patient diversity, Electronic Medical Record data) to improve the feasibility and operational relevance of protocols being drafted across TAs.²⁵

“A laundry list of problems currently plagues study protocols. Among them are the imbalance between science and operational viability, trial complexity, overly strict entry criteria, and superfluous data collection for secondary and tertiary endpoints. It is quite scary how much data is collected across the industry that is never actually used.”

- Jason Gubb, Head of delivery optimisation and informatics, Global clinical operations, GSK²⁶



Pursue transformative development approaches

As stated in our 2020 report, master protocols and adaptive trial designs were used widely for the rapid assessment of the effectiveness of repurposed drugs and new therapies against COVID-19.²⁷ The industry should now seize the opportunity to learn the lessons from the use of these transformative approaches to build towards a future where they can be applied selectively across other therapy areas. Doing so requires several operational and cultural changes within R&D biopharma companies including:

- encouraging development teams to experiment and consider where and when these approaches could be applied, especially in areas of high unmet need
- sharing successes, experiences, and lessons from the use of these approaches across the development organisation
- applying master protocols to areas of scientific complexity and unmet need this can expedite study hypothesis testing through use of shared infrastructure and knowledge generation
- engaging early and transparently with regulator review teams to understand their perspective and concerns on the use of these approaches (this is discussed in more detail in our publication - *Bringing new therapies to market: Transforming clinical development*)²⁸



Accelerate the use of digital technologies

The constraints imposed by the pandemic, such as lockdowns and social distancing, led the industry to accelerate the adoption of digital technologies to run hybrid clinical studies and ensure continuity of routine development activity. Many companies leveraged digital technologies to run COVID-19 vaccine trial activities including optimising site selection, recruiting diverse study populations and capturing data from and managing patients remotely. AI-based epidemiological models helped companies analyse RWD such as case numbers, hospitalisations, testing rates and local COVID-19 policies to predict COVID-19 hotspots and optimise site selection. This enabled the recruitment of participants from countries where new variants were surfacing as trials began, collection of data from diverse racial and ethnic groups, and submission of data rich evidence packages to regulators.²⁹

Companies also made use of e-consent, e-diaries, wearables, and data management platforms to capture and manage millions of data points from thousands of participants across different geographies. Additionally, dashboards offering near real time visibility into study conduct and activities (such as site enrolment, randomisation, sample collection, data entry, cleaning, and overall data quality) were used to identify issues, make decisions and adjustments to keep trials moving quickly.³⁰ These examples demonstrate the acceleration in digital transformation envisaged in our 2020 report *Predicting the future of healthcare and life sciences in 2025: Companies have reversed the decline in returns from pharma R&D* including the increased use of AI-enabled technologies.³¹

Our December 2021 report, *Biopharma digital transformation: Gain an edge with leapfrog digital innovation*, which surveyed 150 biopharma leaders, found that the pandemic forced companies to prioritise digital innovation, instil it into every aspect of work and use it to transform the experiences of patients and partners. Eighty-two per cent of survey respondents believe the momentum of digital innovation is likely to continue post-pandemic, suggesting that biopharma is now at a digital innovation inflection point.³²

Many disrupted clinical trials adopted hybrid or decentralised studies across TAs. This required companies to focus on reducing the 'digital learning curve' for site staff and investigators including using virtual reality (VR) and augmented reality (AR) technologies in their operations and deploying virtual study coordinators on site to help staff enhance familiarity with digital tools, understand data workflows, and manage issues with remote data collection. Companies should also minimise the digital burden on patients by assessing the comfort, accessibility, and ability of study populations to use remote assessment tools. This will be essential to ensure a truly seamless clinical trial experience for participants in future clinical studies.

Digital operational dashboards that can evaluate study operations in real-time could provide agility to modify enrolment strategies or criteria as needed to quickly reach recruitment goals. Furthermore, expanding remote data collection requires investing in automation and AI solutions to validate, manage, clean, and integrate large volumes of data before database lock and downstream use.

Strive for greater diversity in clinical trials

COVID-19 has disproportionately affected minority and disadvantaged populations, increasing focus of ensuring equitable representation in COVID-19 studies (see case study 2).

CASE STUDY 2

Enhancing participant diversity in a COVID-19 Phase III study

Genentech’s EMPACTA Phase III study focused on enrolling underserved and minority patients to demonstrate its efficacy in treating COVID-19 associated pneumonia.³⁴ Approximately 85 per cent of the 389 patients were from minority racial and ethnic groups and included Hispanic, Native American and Black populations.

To achieve this diverse enrolment, Genentech first identified COVID “hotspots” and then analysed epidemiology data to find communities and hospitals where underrepresented patients were being treated. This included areas in New Orleans, New Mexico, and Arizona as well as hospitals in the Bronx where the disease burden was high for underserved populations. After the study sites were identified, enrolment was the fastest among all studies in the history of Genentech, disproving the notion that it takes more time to recruit diverse study populations.³⁵

There is now a growing commitment among biopharma companies to foster clinical trial diversity and ensure study populations match the prevalence of disease across racial and ethnical groups.

Deloitte’s recent research with the Pharmaceutical Research and Manufacturers of America (PhRMA) on strategies to enhance diversity in clinical trials identified four focus areas for companies to expand on this commitment.³³ These include:

01. Identifying and developing alternative clinical sites focused on treating underrepresented populations: Increasing enrolment and retention of diverse trial populations requires meeting patients where they are and working with health care providers they already trust. Leveraging alternate sites such as clinics, pharmacies, military health institutions, and minority-serving institutions, could have a notable impact on the inclusion of underrepresented populations in clinical studies.

02. Developing and training diverse investigators and site staff: Patients tend to trust providers who look like them, so companies and researchers should work on attracting physicians from underrepresented populations to participate in clinical research and create opportunities for them to serve as clinical trial investigators.

03. Building community relationships: Companies and sponsors should work with the community to build longstanding bi-directional relationships that expand beyond the transactional nature of any one clinical trial and focus those relationships on elevating health equity in the community overall.

04. Establishing measures and metrics for success: Building tools to assess participant enrolment by ethnicity and race in real time can aid in recruitment, engagement, and retention of a diverse study population.

COVID-19 has broadened the cohort focus on infectious diseases with vaccines likely to dominate expected revenues for several years

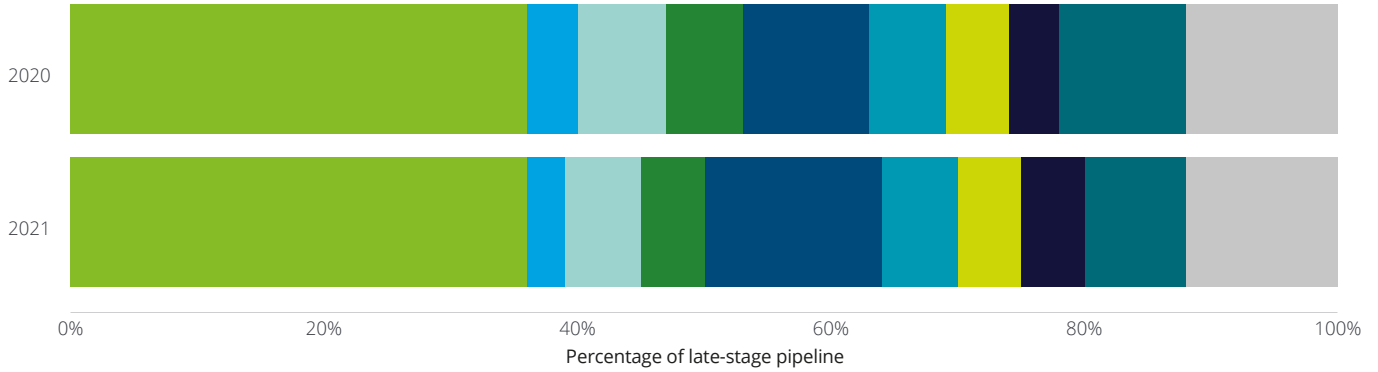
As in previous years, we analysed the TA focus of our combined cohort of 15 companies (see Figure 12). This shows that the proportion of the pipeline focused on infectious disease assets has grown by four percentage points since 2020. Meanwhile the relative proportion of late-stage assets in metabolic, cardiovascular, central nervous system and immunology all declined slightly (by around one percentage point).

The increased proportion of infectious disease assets is primarily due to a surge in the number of COVID-19 vaccines and therapies under development, which have more than tripled since our 2020 analysis period. Importantly, the pandemic has raised the profile of the significant role of vaccines as a tool for public health, with vaccine R&D attracting increasing attention and funding from companies and governments.

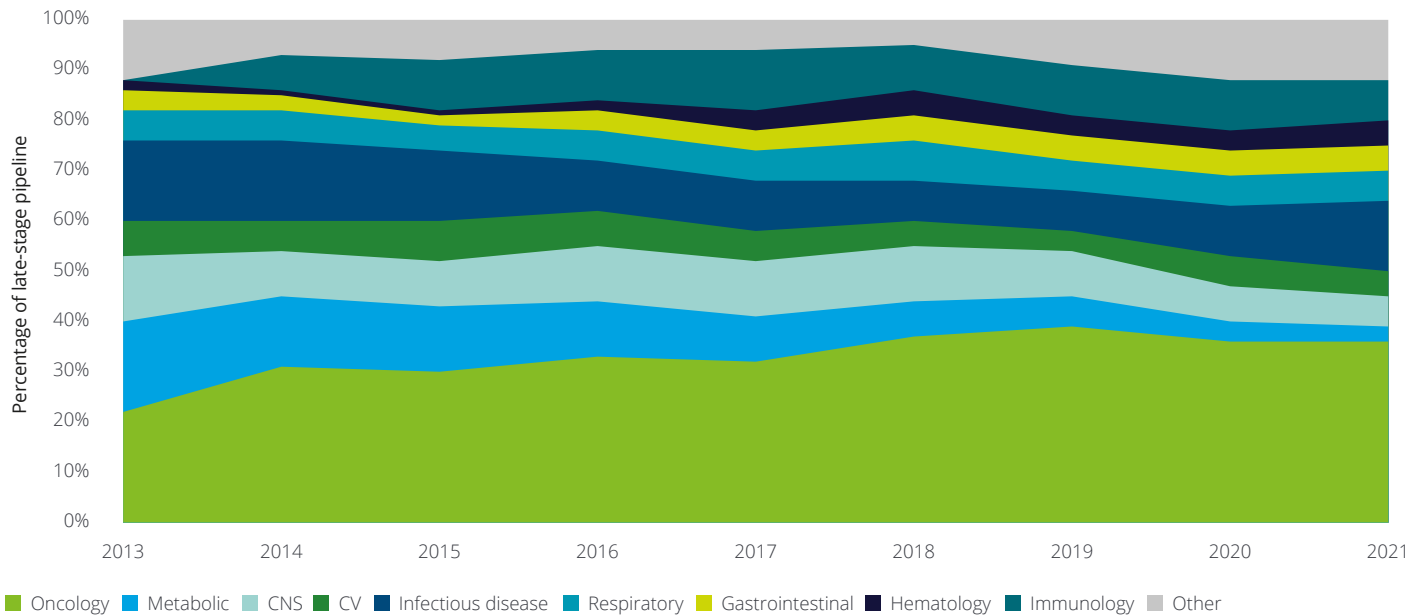
This could lead to the development of a broader arsenal of vaccines for a wide range of diseases over the next few years. In fact, eight companies in the combined cohort are also developing therapies and vaccines for other infectious diseases such as HIV, respiratory syncytial virus infections, pneumonia, and dengue. Additionally, there are several early-stage assets being developed to combat infectious diseases including tuberculosis, hepatitis, and shigella infections that are outside the scope of our analysis.



Figure 12. Late-stage pipeline composition by TA
Top 20 R&D companies, 2020-21



Combined cohort, 2013-21



Source: Deloitte LLP, 2021

Furthermore, companies in our combined cohort are already adapting mRNA technology to create novel and more effective vaccines for other diseases. Pfizer is currently testing the safety of its mRNA vaccine for influenza (see case study 3), while Roche is conducting a Phase II study of its novel personalised mRNA vaccine for melanoma and solid tumours.^{36,37} mRNA technology is also likely to remain important in expediting the effective development of vaccines against any new COVID-19 variants of concern emerging across the globe.

Our analysis of the combined cohort also suggests that vaccines are likely to dominate expected revenues across different modality types over the next few years.

CASE STUDY 3

Creating next generation influenza vaccines using mRNA technology

Influenza causes approximately five million cases of severe illness and up to 650,000 deaths worldwide every year.³⁸ Current traditional vaccines typically confer 40 to 60 per cent protection against circulating influenza strains, that are actively mutating.³⁹ Manufacturing such vaccines involves identifying the correct strains for seasonal vaccine production six months in advance, keeping up with viral strain changes, and altering vaccine antigens during production.

The flexibility of mRNA vaccine technology (that uses a genetic sequence of the viral strain to develop a vaccine) enables accurate strain selection closer to the influenza season. Added advantages include ease of modification and incorporation of a larger number of antigens for greater immunity as well as the ability to quickly scale production in case of larger outbreaks.⁴⁰

As COVID-19 vaccination programmes expand across the globe, to include younger populations and booster dosing, revenues from COVID-19 vaccines for our cohort are only likely to grow.

Our analysis suggests revenues from vaccines (including COVID-19 vaccines with emergency approval status) are expected to reach \$47 billion by 2025, primarily driven by sales of Pfizer's COVID-19 vaccine. New vaccines, such as those for HIV and dengue that are also likely to enter the market soon, will also contribute to these forecast revenues.

Nurturing growth and sustaining the momentum of change

Navigating the impact of the pandemic has been an all-encompassing, once-in-a-generation, challenge for the biopharma industry. While the industry rose to the occasion by making innovative changes to the R&D process, now is the time to sustain the momentum of change to prepare for the future. Success will depend on the industry's ability to learn the lessons from the use of transformative trial design and roll-out, cross industry collaborations, and the adoption of digital solutions to maintain and institutionalise new ways of working for the future.

We have identified four over-arching areas which companies should focus on to nurture the growth identified by our 2021 analysis and create a more productive future for R&D. This should include driving more equitable and quicker access to new therapies and engendering greater trust in the industry.

Unlock the power of collaborative data sharing: Advances in data science, analytics and digital technologies have created the ideal conditions to use the transformative power of data to improve R&D productivity. The pandemic has proved the value and benefit of pre-competitive data sharing in the spirit of collaboration. Expanding this to other disease areas such as Alzheimer's and HIV could enable companies to build on prior and emerging knowledge and reduce duplication of research efforts to accelerate development.

This should be supported by investments in cloud-based capabilities to access, analyse, and share data that is traditionally locked in silos.

Companies should also convene RWD ecosystems to better understand disease, inform patient centric protocol design, and expand the use of real-world evidence (RWE) in regulatory submissions. Collaborations with multiple stakeholders (health systems, patients, patient groups) across geographies will be crucial to curating research-grade RWD while putting in place governance for data access, privacy, and security.

Build a digital talent pool: Our 2021 *Biopharma Digital Innovation* study emphasises that acquiring the right 'digital talent' (such as data scientists, cloud engineers and other technology experts) is key to accelerating digital transformation.⁴¹ For drug development, creating a digital talent pool is essential to expand use of data science-driven and hybrid study approaches in the coming years.

Such talent is highly sought after and increasingly being developed and nurtured by start-ups, technology companies, and academia. This highlights the need for companies to rethink talent strategies and create alliances within the innovation ecosystem to access digital talent at source. Aligning data scientists and technology experts to a therapy area can help cultivate a digital talent pool with a nuanced understanding of drug development. Additionally, companies should also invest in reskilling existing talent to enable them to adapt to the accelerated pace of digital technology integration in development operations.

Trust, health equity, and patient centricity: Building trust is not a one-off activity but the result of cumulative actions and behaviours. The pandemic has provided the biopharma industry with a unique opportunity to connect with patients globally by showcasing its innovative capabilities and value to society.

The industry can now build on this connection in several ways, including improving health equity through a deeper focus on ensuring that patients enrolled in clinical trials match the racial and ethnic diversity of populations affected by the disease in question. Such studies could provide participants access to the latest therapeutic interventions and high-quality care that they might not otherwise have access to. At the same time, the ability to assess safety and efficacy responses in representative and diverse populations could improve public trust and build confidence in therapies once they are launched into the market.

Our research indicates that when a biopharma company demonstrates certain behavioural signals (humanity, transparency, capability, and reliability), consumers will view their brand more favourably. Accordingly, our *Overcoming biopharma's trust deficit* report outlines strategies that can help companies strengthen these signals and gain consumer trust: including devoting more efforts to support communications that clearly explain complex science and trials to the public including how drugs are developed, trial outcomes and the effectiveness and/or side effects.⁴²

Today, more than two billion people worldwide have no access to essential medicines as medicines may be unaffordable, unavailable, inaccessible or non-quality assured.⁴³ Furthermore, the increased awareness (due to the COVID-19 pandemic) of the impact of both global and national health inequalities on health outcomes, mean there is a need for much better awareness and more targeted action to improve access to medicine for all. As demonstrated in our analysis of over 400 access and affordability programmes (AAP), these programmes can provide equitable and sustainable access to medicines and health care around the world.⁴⁴

These programmes enable biopharma companies to improve equity by delivering better outcomes through improved access helping to reduce health inequalities and promote greater investment, visibility and transparency across the industry.⁴⁵

Integrate environment, social, governance (ESG) and purpose-led sustainability initiatives into R&D:

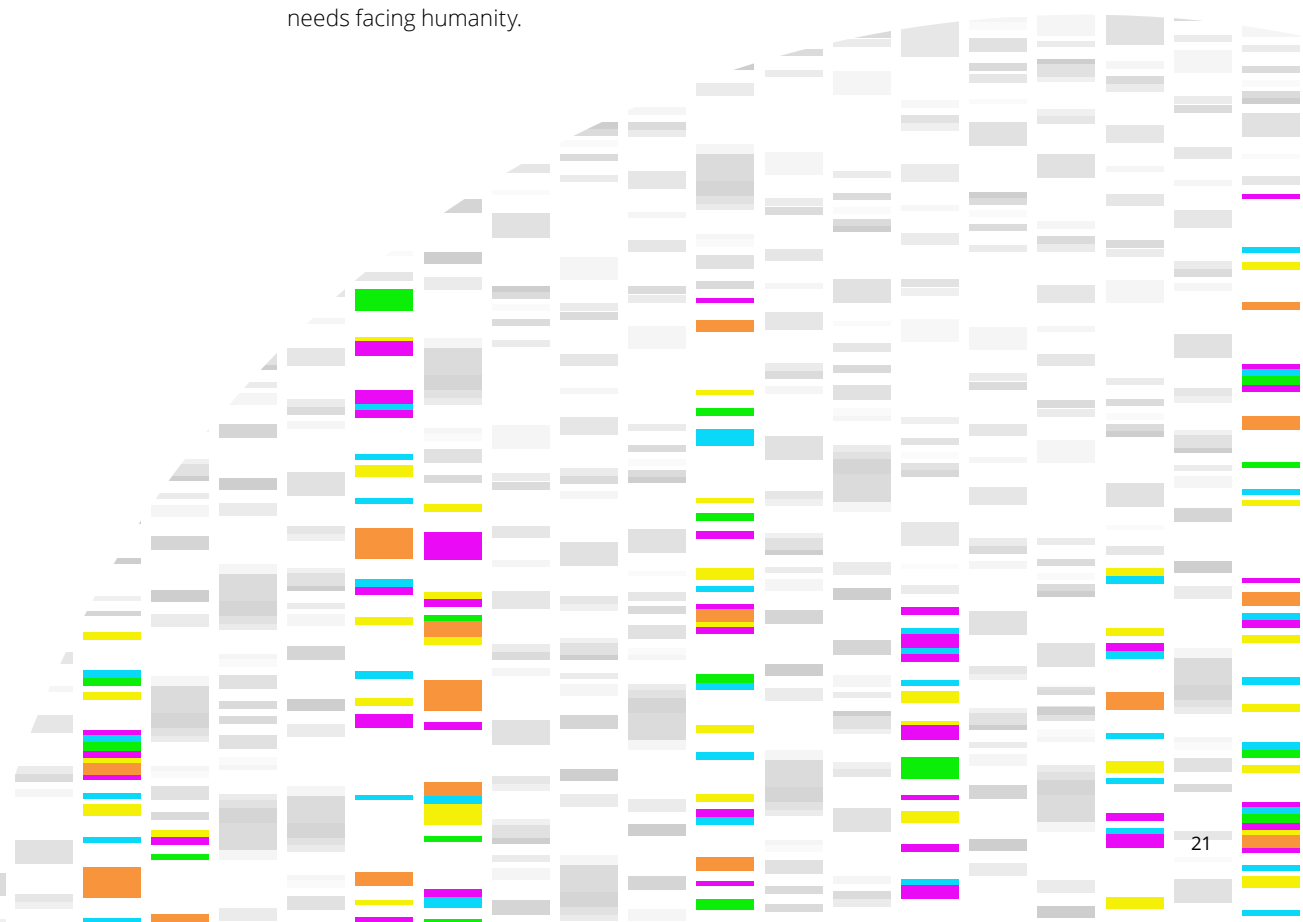
COVID-19 has shone a spotlight on the importance and impact of businesses having a shared purpose and common goal to achieve beneficial outcomes. As a result, stakeholders including regulators, investors and employees are increasingly encouraging companies across industries to drive purpose-driven efforts around improving the environment, social good, and transparent governance.⁴⁶ The Science Based Targets initiative (SBTi) launched in September 2020 to develop the first science-based global standard for corporate net-zero target-setting, consistent with achieving a net-zero world by no later than 2050 has resonated widely across industries.⁴⁷ Companies that adopt ESG imperatives and embed purpose-led initiatives can be more adaptable, resilient and better serve the demands of stakeholders while gaining competitive advantage.

The research evidence is unequivocal: public, planetary and economic health are inextricably linked, and no continent, country or community is immune from the impacts of climate change.⁴⁸

R&D leaders should consider how clinical trials, with increased diversity, are designed and how their complex supply chains impact and contribute to the carbon footprint. The undeniable overlap between environmental and societal health places biopharma companies in a unique position to create a connected strategy that is driven by purpose and a transparent commitment to society to build trust and engagement across the population. In addition to sustainability impacts, biopharma companies can have a tangible impact on health equity, human health and societal good by purposefully driving the use of their innovation portfolios towards health equity in all its forms.

The level of maturity of engagement varies significantly across biopharma companies with many becoming increasingly ambitious in their environmental commitments.⁴⁹ While most life sciences companies have made material global public health investments and address major areas of societal unmet medical need, company leadership and their Boards should develop further to continuously reflect on where R&D spend is being allocated and strive to proactively align and tailor investments to the most prominent unmet needs facing humanity.

The COVID-19 pandemic has inexplicably demonstrated the importance of collaboration and co-investment between governments, academia, and industry to achieve an unparalleled pace of change. With patients engaging in their health more than ever before and biopharma companies becoming household names, societies' and patients' expectations about equity of access and treatment has increased. Additionally, the pandemic has exposed healthcare's vulnerabilities and and threats to equality in healthcare so ESG driven changes need to be considered in tandem with how it might affect the resilience and sustainability of healthcare in the future.⁵⁰



Appendix 1. Methodology

Since 2010, our *Measuring the return from pharmaceutical innovation* series has focused on the projected returns from the late-stage pipelines of a cohort of the 12 largest biopharma companies. Since 2015, we have also included an extension cohort of four mid-to-large cap, more specialised companies, with data retrospectively calculated back to 2013. Following the acquisition of an extension cohort company by a company in our original cohort, and the convergence in performance of the cohorts, we combined these two cohorts to form a 'combined cohort' in 2020.

Our consistent and objective methodology focuses on each company's late-stage pipeline (assets that are filed, in Phase III or Phase II with breakthrough therapy designation as of 30th April each year) and measures performance across the combined cohort of companies. We use two inputs to calculate the Internal Rate of Return (IRR): 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. Assets with emergency use approval such as the COVID-19 vaccines and therapies, are considered to still be part of the late-stage pipeline as are the costs of developing these assets.

As assets are approved, forecast revenues move from late-stage pipeline into the commercial portfolio, moving out of the scope of our analysis and decreasing

the value of the late-stage pipeline. Our analysis accounts for multiple factors including forecast revenue splits where a 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; and the impact of clinical cycle times. 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.

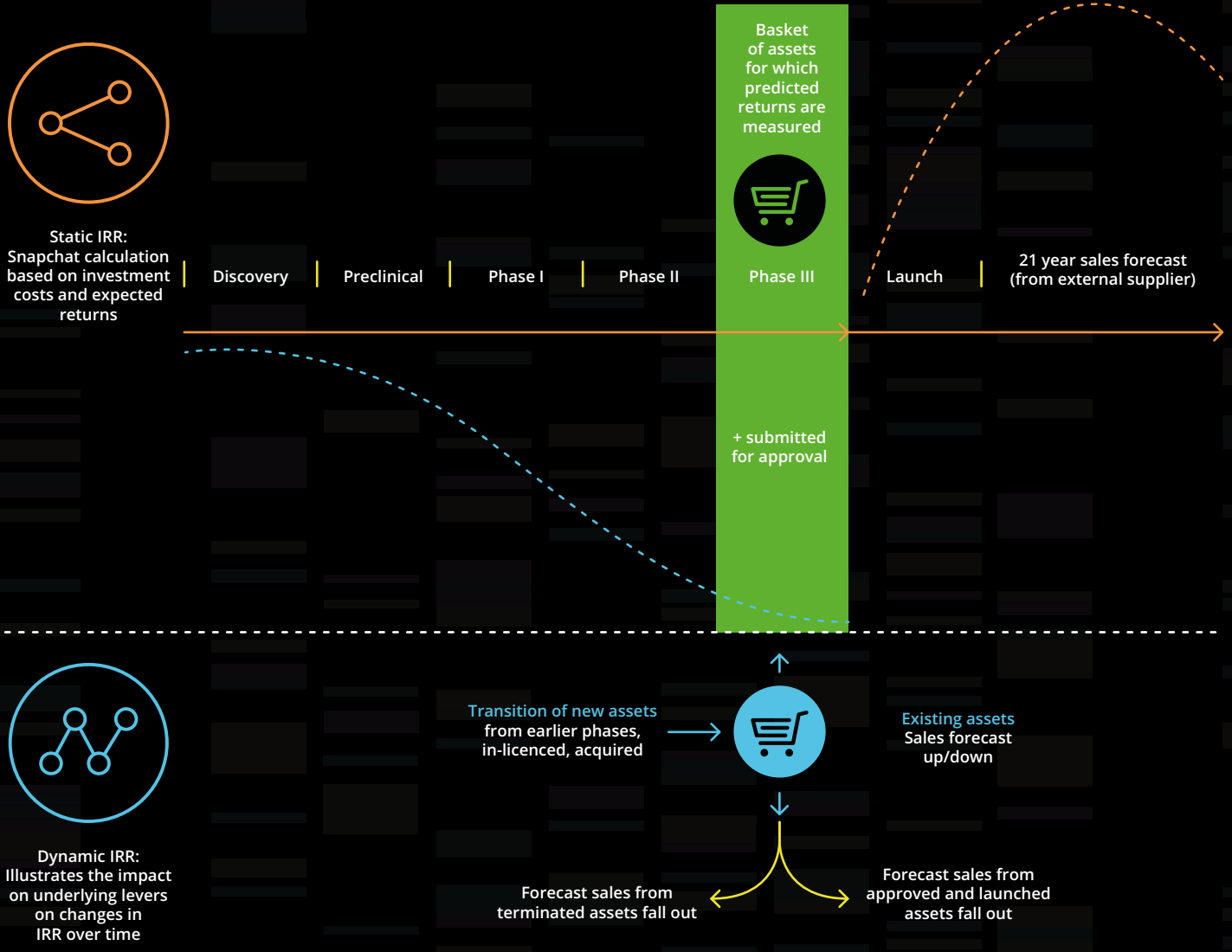
Therefore, our calculations of the total spend incurred in developing and launching assets include the expenditure on terminated programmes and compounds.

Importantly it should be noted that we are continually working to improve the methodology and modelling underpinning this analysis and reviewing the assets included in our pipeline year-on-year

to ensure accuracy and continuous improvement. Therefore, some numbers have been restated, but the same consistent and objective methodology is applied across all cohort companies each year.

The graphic on the following page illustrates our methodology, showing both the static and year-on-year dynamic (three-year rolling average) measures of R&D returns. The three-year average figure, first introduced in our 2015 report, 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.

Late-stage pipeline static IRR and drivers of change in IRR methodology

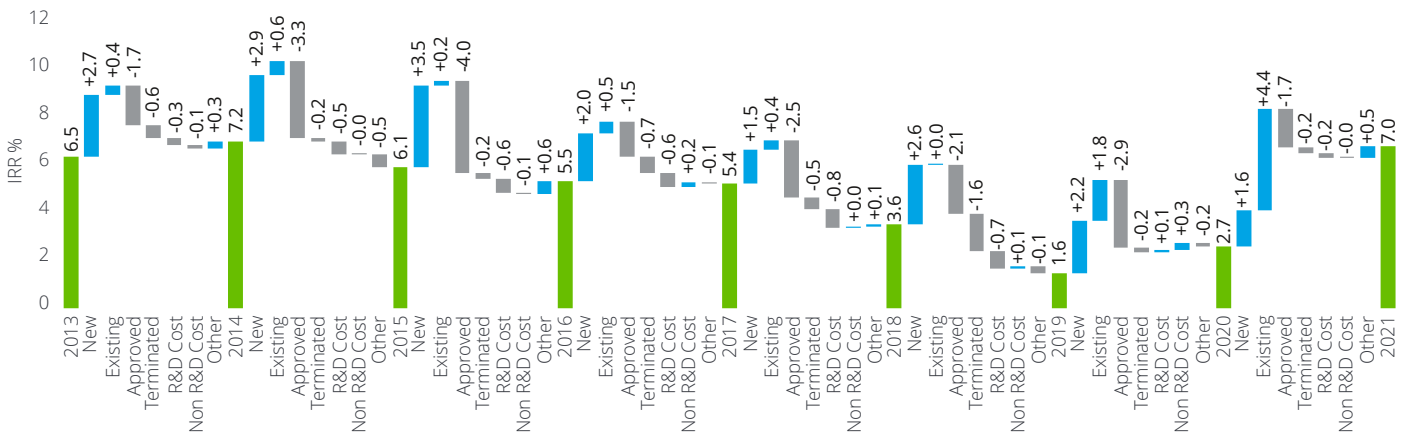


Source: Deloitte LLP, 2021.

Over the past two years, we have started to analyse the performance of a further five companies to extend our analysis to the top 20 R&D biopharma companies by R&D spend to give a more accurate picture of the overall industry. The intention in to include these companies from next year we have enough data points (minimum of three years) to analyse the trend.

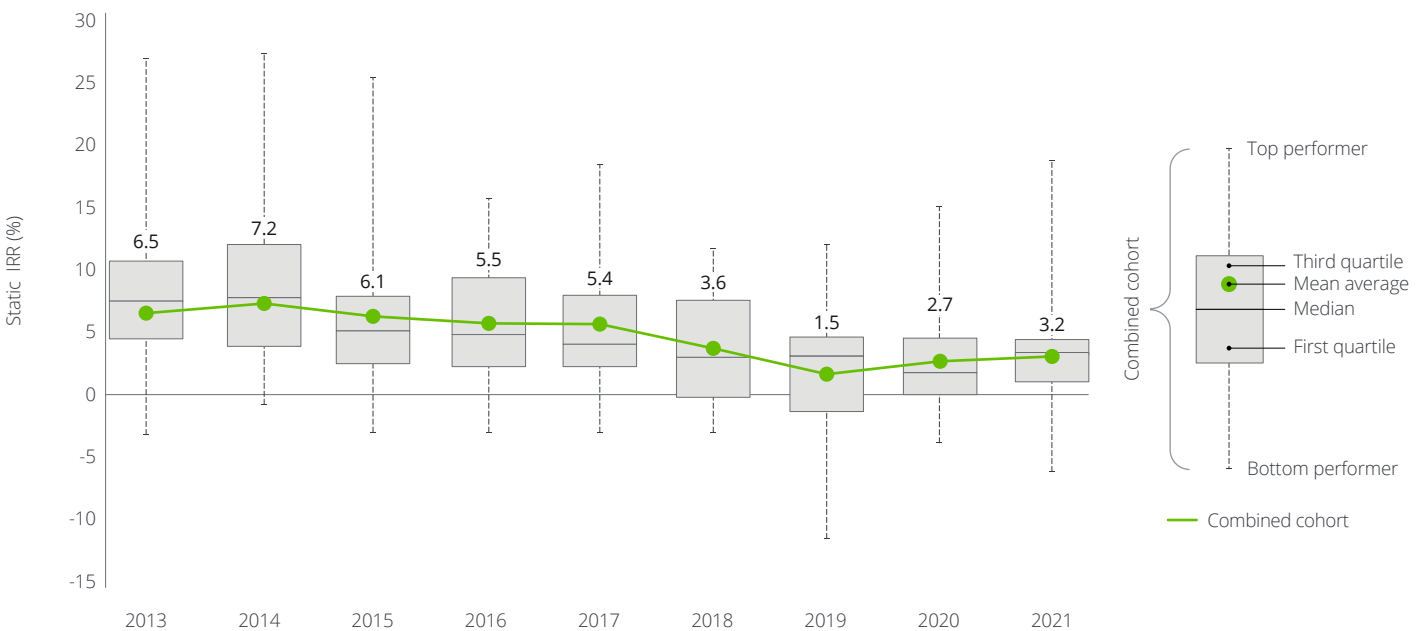
Appendix 2. Additional analyses of the R&D IRR data

Figure 14. Year-on-year drivers of change in IRR, 2013-21 - combined cohort



Source: Deloitte LLP, 2021

Figure 15. Return on late-stage pipeline, 2013-21 - combined cohort without COVID-19 emergency-approval assets



Source: Deloitte LLP, 2021

Endnotes

1. Ten years on: Measuring the return from pharmaceutical innovation, Deloitte LLP, January 2020. See also: <https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-ten-years-on-measuring-the-return-2019.pdf>
2. Seeds of change: Measuring the return from pharmaceutical innovation, Deloitte LLP, May 2021. See also: <https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-measuring-the-return-from-pharmaceutical-innovation-2021.pdf>
3. Kezia Parkins, OCT West Coast: Covid-19's impact on clinical trials, Clinical Trials Arena, 2 March 2021. See also: <https://www.clinicaltrialsarena.com/analysis/covid-19s-impact-on-clinical-trials-oct-west-coast/>
4. Seeds of change: Measuring the return from pharmaceutical innovation, Deloitte LLP, May 2021. See also: <https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-measuring-the-return-from-pharmaceutical-innovation-2021.pdf>
5. 2021 global life sciences outlook: Possibility is now reality, sustaining forward momentum, Deloitte, April 2021. See also: <https://www2.deloitte.com/global/en/pages/life-sciences-and-healthcare/articles/global-life-sciences-sector-outlook.html>
6. Enhancing public trust in COVID-19 vaccination: The role of governments, Organisation for Economic Co-operation and Development (OECD), 10 May 2021. See also: <https://www.oecd.org/coronavirus/policy-responses/enhancing-public-trust-in-covid-19-vaccination-the-role-of-governments-eae0ec5a/>
7. Els Torreele, Mariana Mazzucato and Henry Lishi Li, Delivering the people's vaccine: Challenges and proposals for the biopharmaceutical innovation system, UCL Institute for Innovation and Public Purpose, Policy Brief series (IIPP PB 12), January 2021. See also: https://www.ucl.ac.uk/bartlett/public-purpose/sites/public-purpose/files/iipp-pb12_delivering-the-peoples-vaccine_final.pdf
8. A phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals, Pfizer, November 2020. See also: https://cdn.pfizer.com/pfizercom/2020-11/C4591001_Clinical_Protocol_Nov2020.pdf
9. Craig Morgan, Parallelization: imperative to the compression of clinical trial cycle times, Oracle, 19 April 2021. See also: <https://blogs.oracle.com/health-sciences/post/parallelization-imperative-to-the-compression-of-clinical-trial-cycle-times>
10. Wendy Holman et al., Accelerated first-in-human clinical trial of EIDD-2801/MK-4482 (molnupiravir), a ribonucleoside analog with potent antiviral activity against SARS-CoV-2, BioMed Central, 23 August 2021. See also: <https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-021-05538-5>
11. Ibid.
12. Mengya Liu et al., Innovative trial designs and analyses for vaccine clinical development, Contemp Clin Trials, January 2021. See also: <https://pubmed.ncbi.nlm.nih.gov/33227451/>
13. 2021 global life sciences outlook: Possibility is now reality, sustaining forward momentum, Deloitte, April 2021. See also: <https://www2.deloitte.com/global/en/pages/life-sciences-and-healthcare/articles/global-life-sciences-sector-outlook.html>
14. Derrick Gingery, Pink Sheet - After Pandemic, US FDA Commissioner Wants To Continue 'Rolling Review' Offered To COVID-19 Products, Friends of Cancer Research, 13 October 2020. See also: <https://friendsofcancerresearch.org/news/pink-sheet-after-pandemic-us-fda-commissioner-wants-continue-rolling-review-offered-covid-19>
15. Francesca Bruce, EMA's Emer Cooke On The Future Of Rolling Reviews & The End Of Remote Meetings, Pink Sheet: Informa Pharma Intelligence, 22 September 2021. See also: <https://pink.pharmaintelligence.informa.com/PS144983/EMAs-Emer-Cooke-On-The-Future-Of-Rolling-Reviews--The-End-Of-Remote-Meetings?vid=Pharma&processId=e8fd807d-77f8-4ff9-bc47-6556326d044e>
16. BioPharma Companies Announce Formation of Accumulus Synergy, American Pharmaceutical Review, 22 January 2021. See also: <https://www.americanpharmaceuticalreview.com/1315-News/572467-BioPharma-Companies-Announce-Formation-of-Accumulus-Synergy/>
17. Accumulus Synergy: Accumulus Synergy Selects Google Cloud to Support Its Global Information Exchange Platform and Transform How, Bloomberg, 5 August 2021. See also: <https://www.bloomberg.com/press-releases/2021-08-05/accumulus-synergy-accumulus-synergy-selects-google-cloud-to-support-its-global-information-exchange-platform-and-transform-how>
18. 2021 Life sciences regulatory outlook: Navigating key trends in life sciences regulatory compliance, Deloitte. See also: <https://www2.deloitte.com/us/en/pages/regulatory/articles/life-sciences-regulatory-outlook.html>
19. Randomised Evaluation of COVID-19 Therapy (RECOVERY), University of Oxford, accessed 21 December 2021. See also: <https://www.recoverytrial.net/>
20. Randomised evaluation of COVID-19 therapy (RECOVERY), RECOVERY, 18 June 2020. See also: <https://www.recoverytrial.net/files/recovery-protocol-v7-0-2020-06-18.pdf>
21. Asher Mullard, RECOVERY 1 year on: a rare success in the COVID-19 clinical trial landscape, Springer Nature, 16 April 2021. See also: <https://www.nature.com/articles/d41573-021-00068-w>
22. International sites, RECOVERY and University of Oxford, accessed 21 December 2021. See also: <https://www.recoverytrial.net/international>
23. Clinical Trial Complexity Levels Show Unrelenting Increase, ACRP, 5 May 2021. See also: <https://acrpnnet.org/2021/05/05/clinical-trial-complexity-levels-show-unrelenting-increase/>

24. Ibid.
25. Jason Gubb et al., GSK's Innovative Protocol Design Lab: Challenging the status quo during protocol design and study delivery planning, GSK. See also: <https://cdn.sanity.io/files/0vv8moc6/act/8e3286b3e696b560e6dcb0ec840a0504153c76e3.pdf/ArticulateSpecs.pdf>
26. Deborah Borfitt, GSK's Protocol Design Lab Offers Actionable Insights To Study Teams, Clinical Research News, 18 February 2021. See also: <https://www.clinicalresearchnews.com/news/2021/02/18/gsk-s-protocol-design-lab-offers-actionable-insights-to-study-teams>
27. Seeds of change: Measuring the return from pharmaceutical innovation, Deloitte LLP, May 2021. See also: <https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-measuring-the-return-from-pharmaceutical-innovation-2021.pdf>
28. Andrew Bolt et al., Bringing new therapies to patients: Transforming clinical development, Deloitte Insight, 18 November 2020. See also: https://www2.deloitte.com/content/dam/insights/us/articles/6856_CHS-Accelerating-clinical-development/DL_CHS-accelerating-clinical-development.pdf
29. Terri Park, Behind Covid-19 vaccine development, Massachusetts Institute of Technology (MIT), 18 May 2021. See also: <https://news.mit.edu/2021/behind-covid-19-vaccine-development-0518>
30. The Impact of Digital Technologies in Transforming and Accelerating Vaccine Trials, Development and Delivery – Lessons from COVID-19: Webinar, The Galien Foundation, 17 February 2021. See also: <https://www.galienfoundation.org/index.php/digital-health-webinars-2021/>
31. Companies have reversed the decline in the returns from pharma R&D: Predicting the future of healthcare and life sciences in 2025, Deloitte LLP, December 2020. See also: <https://www2.deloitte.com/uk/en/pages/life-sciences-and-healthcare/articles/companies-have-reversed-the-decline-in-the-returns-from-pharma-r-and-d.html>
32. Aditya Kudumala et al., Biopharma digital transformation: Gain an edge with leapfrog digital innovation, Deloitte Insights, 8 December 2021. See also: <https://www2.deloitte.com/uk/en/insights/industry/life-sciences/biopharma-digital-transformation.html>
33. Alexandria Younossi et al., Enhancing clinical trial diversity: Stakeholder perspectives on advancing research through representative clinical trials, Deloitte Insights, 11 November 2021. See also: <https://www2.deloitte.com/us/en/insights/industry/life-sciences/lack-of-diversity-clinical-trials.html>
34. Genentech's Phase III EMPACTA Study Showed Actemra Reduced the Likelihood of Needing Mechanical Ventilation in Hospitalized Patients With COVID-19 Associated Pneumonia, Genentech, 17 September 2020. See also: <https://www.gene.com/media/press-releases/14881/2020-09-17/genentechs-phase-iii-empacta-study-shows>
35. Ibid.
36. Product Development Portfolio, Roche, 10 October 2021. See also: https://www.roche.com/research_and_development/who_we_are_how_we_work/pipeline.htm
37. Pfizer begins study of mRNA flu vaccine, Reuters, 28 September 2021. See also: <https://www.reuters.com/business/healthcare-pharmaceuticals/pfizer-begins-study-mrna-flu-vaccine-2021-09-27/>
38. Abraham Palache, Flu can cause up to 650,000 deaths a year globally, IFPMA, 27 June 2019. See also: <https://www.ifpma.org/global-health-matters/flu-can-cause-up-to-650000-deaths-a-year-globally/>
39. CDC Seasonal Flu Vaccine Effectiveness Studies, Centers for Disease Control and Prevention, 26 August 2021. See also: <https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm>
40. Rachel Arthur, Pfizer's mRNA flu vaccine candidate set to enter clinic, BioPharma Reporter, 16 September 2021. See also: <https://www.biopharma-reporter.com/Article/2021/09/16/Pfizer-mRNA-flu-vaccine-candidate-set-to-enter-clinic>
41. Aditya Kudumala et al., Biopharma digital transformation: Gain an edge with leapfrog digital innovation, Deloitte Insights, 8 December 2021. See also: <https://www2.deloitte.com/uk/en/insights/industry/life-sciences/biopharma-digital-transformation.html>
42. Greg Reh et al., Overcoming biopharma's trust deficit, Deloitte Insights, 6 May 2021. See also: <https://www2.deloitte.com/uk/en/insights/industry/life-sciences/trust-in-biopharmaceutical-companies-covid.html>
43. Sachiko Ozawa et al., Access to medicines through health systems in low- and middle-income countries, Health Policy and Planning, 09 December 2019. See also: https://academic.oup.com/heapol/article/34/Supplement_3/iii1/5670624
44. Elizabeth Hampson et al., Access and Affordability Programmes: Reducing inequalities in access to medicines, Deloitte LLP, November 2021. See also: Access and Affordability Programmes: Reducing inequalities in access to medicines, Deloitte LLP, November 2021.
45. Ibid.
46. Biopharma Investor ESG Communications Guidance 2.0, The Biopharma Investor ESG Communications Initiative, April 2020. See also: <https://biopharmasustainability.com/wp-content/uploads/Biopharma-Investor-ESG-Communications-Guidance-Apr2020.pdf>
47. Science Based Targets Initiative Developing Global Standard for Corporate Net-Zero Targets, Sustainable Brands, accessed 15 December 2021. See also: <https://sustainablebrands.com/read/defining-the-next-economy/science-based-targets-initiative-developing-global-standard-for-corporate-net-zero-targets>
48. Giles Dean and James Gregson, COP26 – Our hopes for a healthier, collaborative, interconnected future, Deloitte LLP, 3 November 2021. See also: <https://blogs.deloitte.co.uk/health/2021/11/cop26-our-hopes-for-a-healthier-collaborative-interconnected-future.html>
49. ESG Trends and Practices in the Biopharma Industry, PhrmaExec, 14 June 2021. See also: <https://www.pharmexec.com/viewesg-trends-and-practices-in-the-biopharma-industry>
50. Why health system resilience is key to a sustainable future, AstraZeneca, accessed 15 December 2021. See also: <https://www.astrazeneca.com/what-science-can-do/stories/why-health-system-resilience-is-key-to-a-sustainable-future.html>

Contacts

Authors

Emily May

Assistant Manager

UK Centre for Health Solutions
Deloitte LLP
+44 (0) 20 7007 5694
elmay@deloitte.co.uk

Karen Taylor

Director

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

Maria João Cruz

Senior Consultant

Monitor Deloitte
+44 (0) 20 7303 4434
mariajoaocruz@deloitte.co.uk

Sonal Shah

Senior Manager

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

Wendell Miranda

Senior Analyst

US Center for Health Solutions
Deloitte Services LP
+1 (615) 209 6896
wmiranda@deloitte.com

Deloitte EMEA contacts

Colin Terry

Partner

UK Life Sciences & Healthcare Consulting Leader

Deloitte LLP
+44 (0) 20 7007 0658
colterry@deloitte.co.uk

James Gregson

Partner

Life Sciences & Healthcare Industry Leader

Deloitte LLP
+44 (0) 20 7007 8856
jgregson@deloitte.co.uk

Hanno Ronte

Partner

Life Science & Healthcare

Monitor Deloitte
+44 (0) 20 7007 2540
hronte@deloitte.co.uk

Deloitte US contacts

Neil Lesser

Principal

US Life Sciences R&D Leader

Deloitte Consulting LLP
+1 (215) 446 4364
nlesser@deloitte.com

Mike DeLone

Principal

US Life Sciences Sector & Consulting Leader

Deloitte Consulting LLP
+1 (215) 299 5230
mdelone@deloitte.com

Greg Reh

Principal

Global Life Sciences & Healthcare Industry Leader

Deloitte Consulting LLP
+1 (215) 997 7559
grreh@deloitte.com

John Haughey

Partner

Global Life Sciences & Healthcare Industry Consulting Leader

Deloitte MCS Ltd
+44 (0) 20 7303 7472
jhaughey@deloitte.co.uk

Nico Kleyn

Managing Partner

Life Sciences & Healthcare for Switzerland and NSE

Deloitte LLP
+41 58 279 8166
nikleyn@deloitte.ch

GlobalData contacts

David Abramson

Global SVP Pharmaceutical Consulting

GlobalData
+44 (0) 20 7832 4343
dabramson@globaldata.com

Deloitte project team

We would like to acknowledge the significant contribution of the following people to the analysis, research and drafting of this report, without which this report would not have been possible: Kevin Dondarski, Naveed Panjwani, Laveshni Reddy, Pratik Avhad, Serdar Bagis, Benjamin Ackland-Snow and Pavithra Rallapalli

GlobalData contributors

We would like to acknowledge the contribution of Roma Garg (Managing Consultant, GlobalData Research Centre), Brooke Wilson (Associate Director, GlobalData Clinical Trials Intelligence) and GlobalData's Therapy Analysis and Database teams

Contact information

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



This publication has been written in general terms and we recommend that you obtain professional advice before acting or refraining from action on any of the contents of this publication. Deloitte LLP accepts no liability for any loss occasioned to any person acting or refraining from action as a result of any material in this publication.

Deloitte LLP is a limited liability partnership registered in England and Wales with registered number OC303675 and its registered office at 1 New Street Square, London EC4A 3HQ, United Kingdom.

Deloitte LLP is the United Kingdom affiliate of Deloitte NSE LLP, a member firm of Deloitte Touche Tohmatsu Limited, a UK private company limited by guarantee ("DTTL"). DTTL and each of its member firms are legally separate and independent entities. DTTL and Deloitte NSE LLP do not provide services to clients. Please see www.deloitte.com/about to learn more about our global network of member firms.

© 2022 Deloitte LLP. All rights reserved.

Designed and produced by 368 at Deloitte. J21661