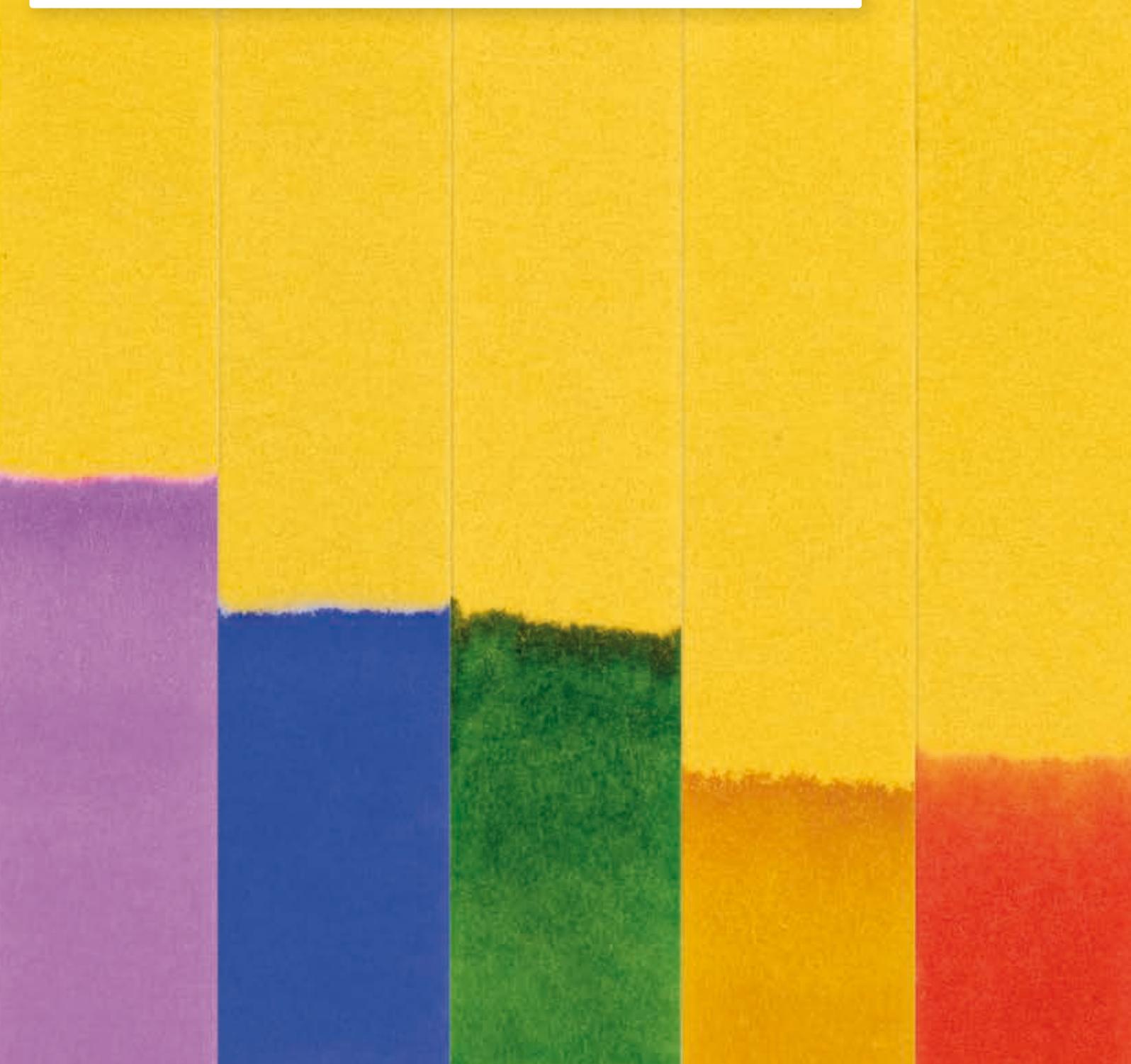


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Deloitte Centre  
for **Health Solutions**

Measuring the return from  
pharmaceutical innovation 2014  
Turning a corner?



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## **The Deloitte Centre for Health Solutions**

The Deloitte Centre for Health Solutions, part of Deloitte UK, generates insights and thought leadership based on the key trends, challenges and opportunities within the healthcare and life sciences industry. Working closely with other centres in the Deloitte network, including the US centre in Washington, our team of researchers develop ideas, innovations and insights that encourage collaboration across the health value chain, connecting the public and private sectors, health providers and purchasers, and consumers and suppliers.

In this publication, references to Deloitte are references to Deloitte LLP, the UK member firm of DTTL.

## **GlobalData**

GlobalData provides world-class healthcare research and consulting that delivers actionable insight and industry perspective on the critical decisions our clients have to make. Together with our experienced team of researchers, analysts, epidemiologists and consultants, and an unmatched suite of proprietary databases and workflow tools, we provide high-quality accurate and transparent insight that helps our clients achieve growth and increase business value. Combining precision with innovation, our research and consulting solutions ensure that our clients stay at the forefront of their markets by integrating forecasts and analysis on the latest trends and developments with the unrivalled expertise of our analyst teams.

# Foreword

Welcome to this Deloitte LLP report, the fifth in our annual series exploring the pharmaceutical industry's performance in generating a return from its significant annual investment in new product innovation.

This report estimates the return on investment that 12 of the leading life science companies might expect to achieve from their late stage pipelines, which comprise assets that should launch within the next three to four years.

The pressure on research and development leaders to identify and successfully develop promising, innovative medicines is relentless. Ongoing austerity measures continue to restrict the ability of healthcare payers to fund new therapies and, at the same time, regulatory scrutiny and scientific uncertainty are having an impact on life science innovators. In spite of these challenges, this year's analysis indicates that over the last five years many of the companies in our cohort have negotiated these hurdles successfully and are continuing to populate their late stage pipelines with promising new compounds and bring new compounds and medical innovation to patients.

Last year, market austerity and affordability were highlighted as the main challenges for life science innovators in the business of R&D. While these challenges remain, this year, our analysis shows that the majority of companies have achieved an improvement in the projected returns from their late stage pipelines, despite a continued rise in the average cost to develop a new product.

In this year's report we examine the underlying factors that could influence returns, for example portfolio mix or focus, company size and R&D spend, and the proportion of science originating from outside the company. We believe this year's report provides further insight to allow R&D leaders to understand the drivers of successful R&D strategies that are tangible and, most importantly, actionable.

We hope you find the report thought-provoking and welcome your feedback on the findings as well as the implications for the industry.



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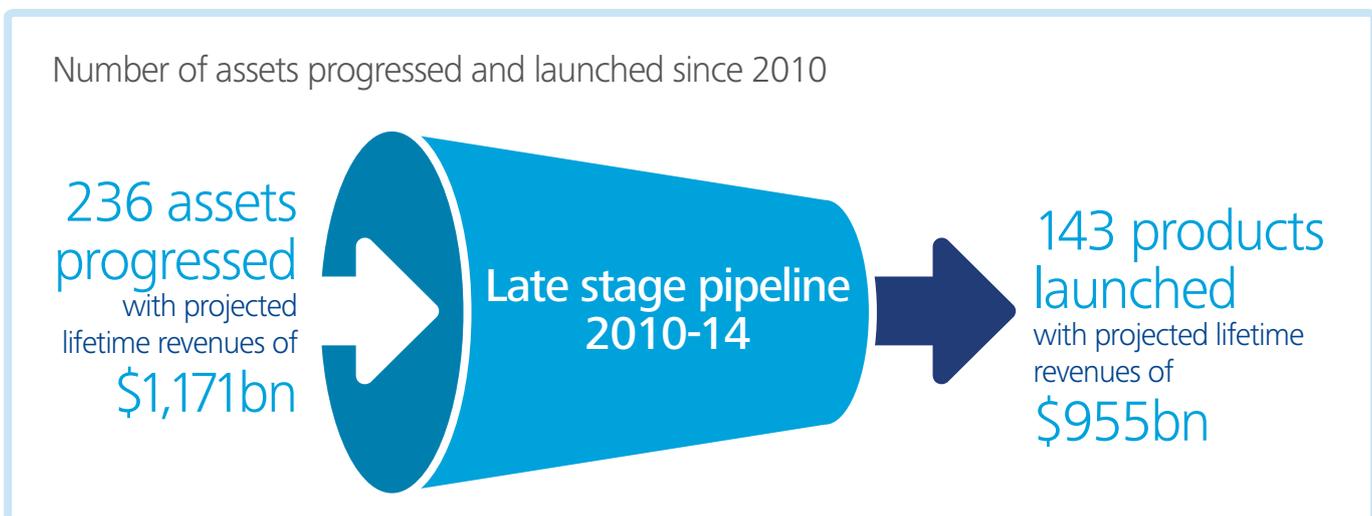
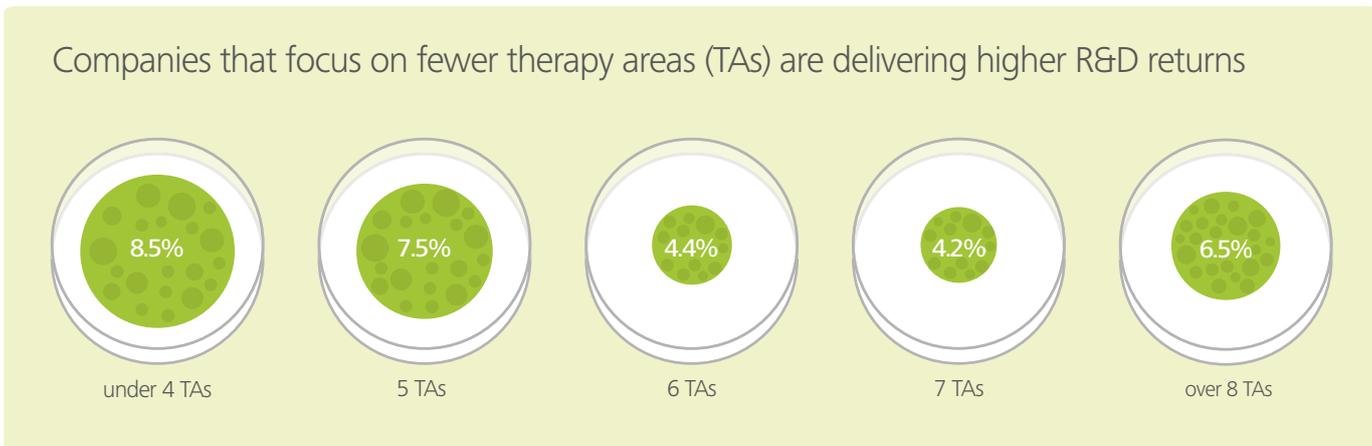
# Size matters as does therapy area focus and external assets have higher sales potential



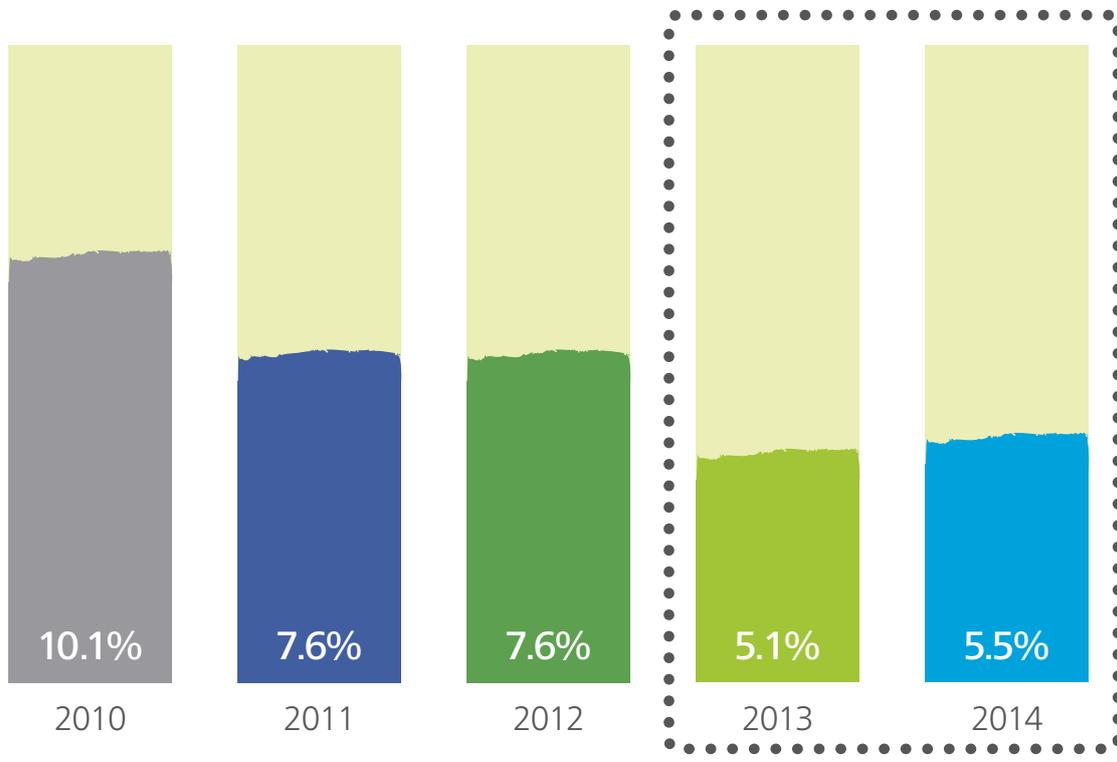
Smaller companies appear to be developing assets more cost effectively and with better returns

Projected peak sales for externally sourced assets are higher:

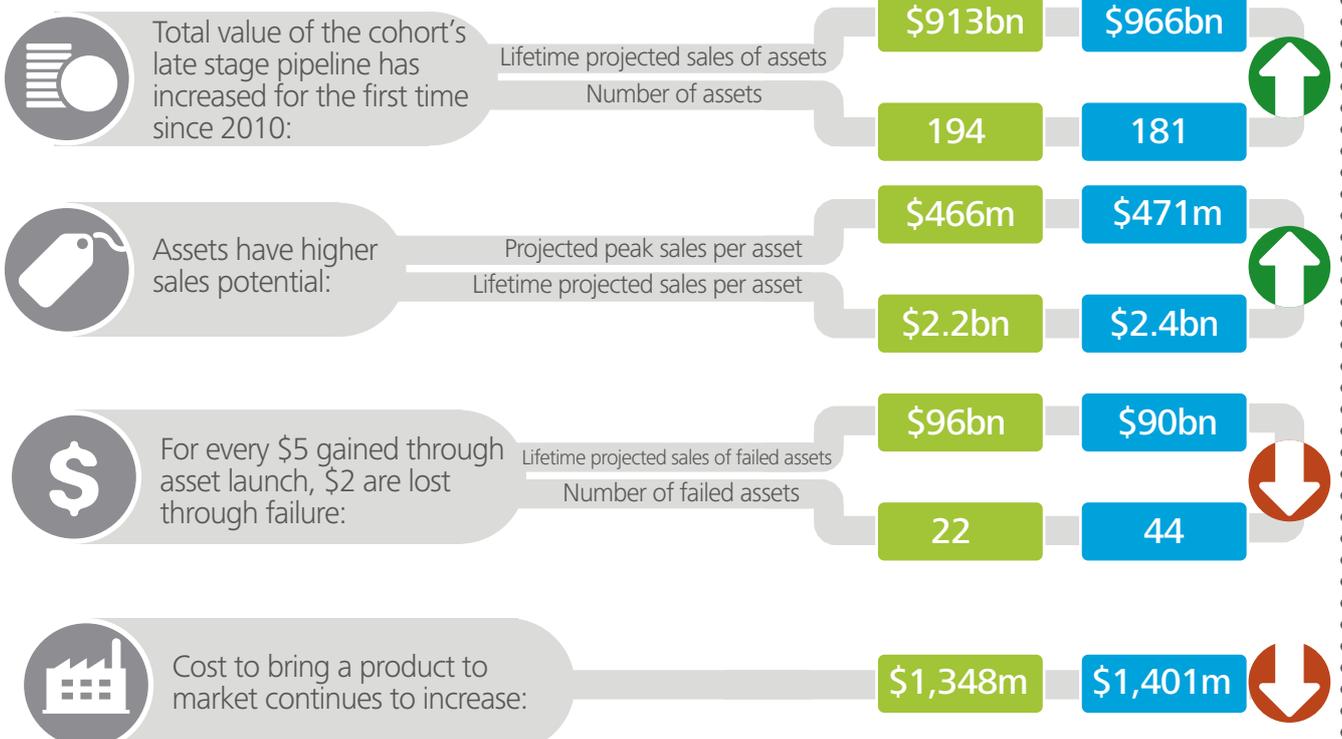
-  +6% for all externally sourced assets
-  +20% for breakthrough assets
-  +54% for orphan drugs



# For the first time since 2010, R&D returns for the cohort have improved



## Key findings from 2014 versus 2013



# Executive summary

Company size, internal or external sourcing of innovation, therapy area focus and R&D functional reorganisations all influence the ability to make profitable returns.

Since 2010, our cohort of 12 life science companies has launched 143 products with total, forecast lifetime sales of \$955 billion. Over the same period, the R&D divisions of these companies have progressed 236 assets into late stage pipelines, with total forecast lifetime sales of \$1,171 billion.

However, R&D costs continue to climb and there has been relatively little change in the value leakage arising from late stage asset terminations. The overall cohort internal rate of return has declined, from 10.1 per cent in 2010 to 5.5 per cent in 2014, but in 2014 for the first time, there has been a halt to the decline and even an uplift in R&D returns relative to 2013. There are signs that the industry is starting to recover some of the ground lost since 2010.

The balance between cash inflows and cash outflows continues to be eroded with the cost of bringing an asset to market, including accounting for failures, rising for the fifth year to \$1,401 million. However, for the first time since 2010 the average forecast revenues of an individual asset have increased, regaining most of the ground lost since 2012. The average forecast peak sales per asset have also recovered slightly, by \$5 million since 2013, an indication that the quality of assets in late stage development is improving.

The dynamics behind the uplift in R&D returns are complex with wide variations at the individual company level. Company size, internal or external sourcing of innovation, therapy area focus and R&D functional reorganisations all influence the ability to make profitable returns. With winners starting to emerge, this report seeks to explain some of the strategies that leading companies are pursuing to outperform their peers. According to our analysis the following variables may have some degree of correlation with R&D returns:

- company size
- externalisation
- portfolio focus.

Company size matters. Our analysis of the top 12 companies reveals that the larger the company, by revenue or R&D spend, the greater the cost to develop each asset and the lower the returns. In addition, companies that pursue a large, broad portfolio of assets without rigorous portfolio management and discipline add significant cost without delivering adequate returns. Legacy investment burdens on larger R&D organisations may be one explanation.

The sheer size, complexity and bureaucracy prevalent within some larger life sciences companies may be overshadowing the benefits of scale. With the current levels of scientific, regulatory and commercial uncertainty associated with drug development, and the challenges they pose to innovators, externalisation will remain a viable option for shifting R&D from a fixed to a variable cost base while improving pipeline quality.

Nine of the 12 companies generate more than half of their forecast late stage pipeline revenues from intellectual property that is acquired externally; in fact 58 per cent of the entire cohort late stage pipeline innovation (by forecast revenues) is sourced externally. Our analysis also shows that forecast revenues from externally sourced assets, on average, are six per cent higher than assets which are self-originated. For those drugs with orphan or breakthrough status, the difference is significantly higher. Innovation strategies founded on collaboration, networking and asset acquisitions continue to grow in importance and impact. The ability to engage in and subsequently manage strategic alliances effectively is a critical success factor in life sciences R&D.

Our findings show that those companies focusing on four or fewer therapy areas are forecast to deliver better returns from their late stage portfolios. A strong therapy area focus appears to provide companies with an in-depth knowledge of disease biology and a comprehensive disease management-based view. Instead of a product-based view, deep therapy area expertise also drives more effective commercial conversations with payers when negotiating price, reimbursement and market access.

The life science R&D ecosystem is undergoing a transformation that has forced the industry to take stock and reinvent how it goes about accessing, fostering and commercialising innovation. Some of our cohort are more advanced in their reinvention and are delivering leading returns, while others are part-way through their journey. What is clear, is that the ability to collaborate across the industry and with all stakeholders remains the imperative if returns are to continue to improve.

# Part 1: Relentless pressure on pharmaceutical R&D

## An evolving market continues to prove challenging for pharmaceutical R&D

The global pharmaceutical market is estimated to be worth in excess of \$1 trillion a year and continues to grow.<sup>1</sup> The United States remains the biggest single market for pharmaceutical products but, like the majority of developed western markets, over the next few years its growth will be subdued compared to that of emerging markets.<sup>2</sup> Drug budgets will continue to be constrained across geographies irrespective of growth as expanding and/or ageing populations absorb the vast majority of any increase in drug budgets.

The challenges faced by life science R&D organisations are outlined in a recent Deloitte Consulting LLP report, "In the face of uncertainty: A challenging future for biopharmaceutical innovation".<sup>3</sup> The report identifies four areas of significant uncertainty having an impact on life science innovators:

- Scientific uncertainty – associated with developing innovative medicines for therapeutic areas (TAs) of high unmet medical need which are typically complex and at an early stage of scientific maturity, and biological entities that are still emerging
- Regulatory uncertainty – regulatory approval processes are becoming increasingly complex, presenting a high degree of uncertainty around review times, pre-approval requirements and post-approval requirements
- Coverage uncertainty – pressure on drug budgets continues unabated, leading to tightened reimbursement policies and causing uncertainty over patient access to new therapies
- Policy and implementation uncertainty – the lack of consensus among policymakers, for example around number of years of market exclusivity for innovative biologics, is raising significant concern within the life science industry. The early launch of biosimilars substantially increases the risk that innovative biologics may not achieve a positive return.

Life science innovation is a time consuming and costly endeavour, but the resulting patient benefits have typically provided a level of financial return which balances the risks. Over recent years this balance has been under increasing pressure: rates of return are declining, costs are increasing and medical innovation is becoming more difficult to source.

To generate sustainable returns in this market, R&D organisations will need to have a clear strategy about how to target and serve unmet patient need profitably. They also need to play their part in complying with existing and new legislation, a responsibility which will continue to grow.<sup>4</sup> The challenges that R&D organisations must address are complex and significant, as are the opportunities for the companies that emerge as winners.

## Measuring returns for pharmaceutical R&D is complex

At its simplest level, predicting the likely returns from a company's pipeline requires two macro inputs: the cost of developing an asset or group of assets and an estimate of the future cash flows these assets could deliver.

Quantifying the cost of developing an asset from discovery through to launch is a significant challenge. R&D companies do not publish this information; indeed, it is difficult for the companies themselves to define the exact cost of each asset as typically assets start life as part of a family of closely-related or similar compounds. For each asset that is launched, there are many that fail. A comprehensive calculation of the return on R&D investment, like that used by Deloitte for this report, needs to recognise costs invested in assets that have failed along the way.

Forecasting the revenues arising from an asset in development is also complex and necessarily approximate. Providing robust forecasts must take into account a number of asset characteristics including efficacy, side effect profile, launch date, patent expiry, target patient population, price and the competitive environment into which it will launch. Until an asset reaches Phase III development, many of these characteristics have a high level of uncertainty. To complicate matters further, forecasts of likely returns change as an asset progresses through development. If relevant trial outcomes for the same or similar compounds across the sector are better than expected the likely returns will increase; however if outcomes are below expectations, forecasts will decline.

Pharmaceutical R&D is a lengthy process, with compounds taking approximately 15 years to progress from discovery to launch. Decisions taken by R&D leaders today are unlikely to deliver measurable results in the short term. Therefore, a longer-term view of R&D returns is more meaningful than measuring yearly returns, which can be skewed by one or two assets with particularly high or low revenue expectations. Forecasts can also change substantially as the asset progresses through late stage development.

Since 2010, Deloitte has been assessing the forecast R&D performance of the 12 leading global life science companies by R&D spend.

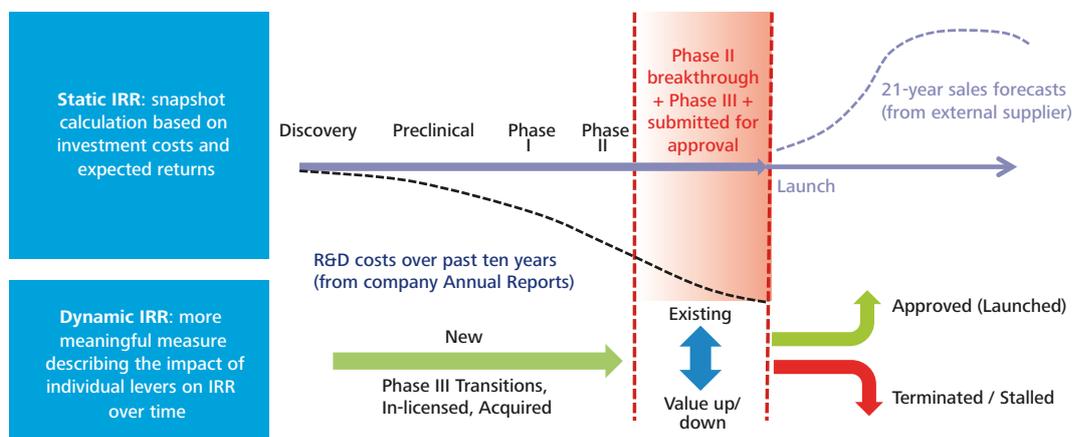
Figure 1 summarises the methodology we have developed and refined to calculate the internal rate of return (IRR) likely to be delivered by a pharmaceutical company's late stage pipeline (see also Appendix: Methodology).

This methodology assesses the impact of a number of drivers on IRR and delivers two key metrics:

- yearly or static IRR – estimating the forecast rate of return at a given point in time
- longer-term or dynamic returns – estimating the impact of different drivers of change in IRR and providing a long-term view of R&D performance.

For the 2014 report GlobalData has provided the revenue forecasts for the late stage pipeline assets. We have improved the methodology used in earlier reports based on feedback from our clients, adjusting the timeframe over which average operating margins are calculated to reflect the impact of recent operational efficiency programmes, and to be as relevant as possible to the economic environment in which the assets are expected to launch. Results published in previous reports have been recalculated to allow for valid year-on-year comparisons.

**Figure 1. Late stage pipeline static IRR and drivers of change in IRR methodology**



Source: Deloitte LLP

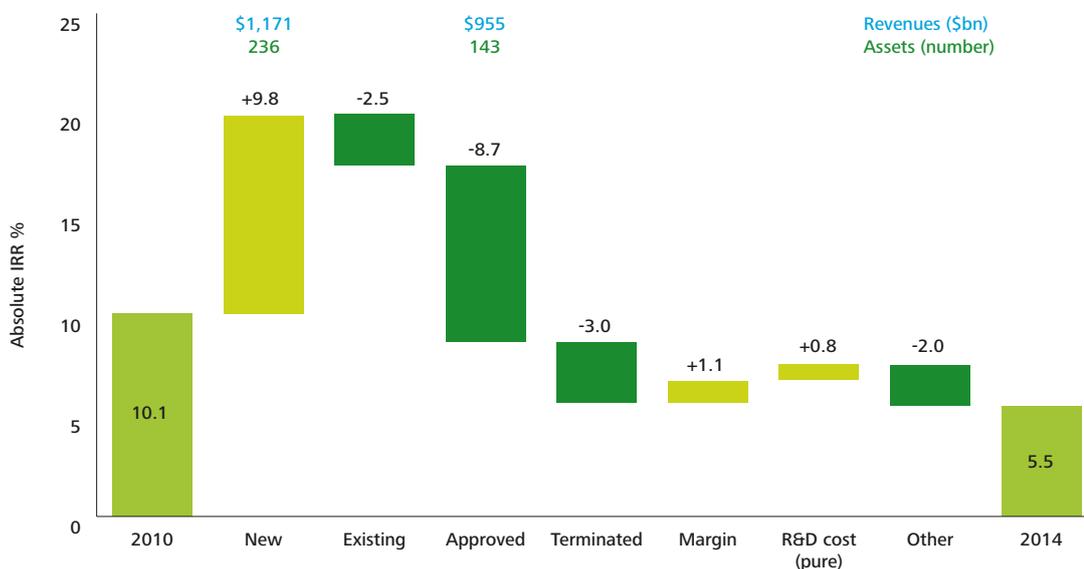
Since 2010, Deloitte has been assessing the forecast R&D performance of the 12 leading global life science companies by R&D spend.

**Overall R&D returns of the leading companies have declined since 2010**

Over the five-year timeframe, from 2010 to 2014, the cohort of 12 companies has launched 143 products with total, forecast lifetime sales of \$955 billion, while their R&D divisions have progressed 236 assets into their late stage pipelines, with total forecast lifetime sales of \$1,171 billion (see Figure 2). Despite these successes, the cohort IRR declined from 10.1 per cent in 2010, to 5.5 per cent in 2014.

Over the five years, the significant value added by new assets entering the pipeline has provided an 'uplift' for the cohort IRR. However, the uplift from new compounds has proven insufficient to replace the sum of value transferred to the commercial portfolio through launches and the value lost due to assets failing or not delivering the commercial outcomes originally anticipated as they progress through late stage development. Slight improvements in operating margin and R&D cost have been offset by other factors such as R&D phasing, licensing costs and tax rates.

Figure 2. Drivers of change in IRR, 2010–14



Source: Deloitte LLP  
Other comprises phasing, licensing costs and tax rates.

Our analysis of year-on-year trends since 2010 shows that the drivers of change in IRR exert different impacts over time (see Figure 3). For example:

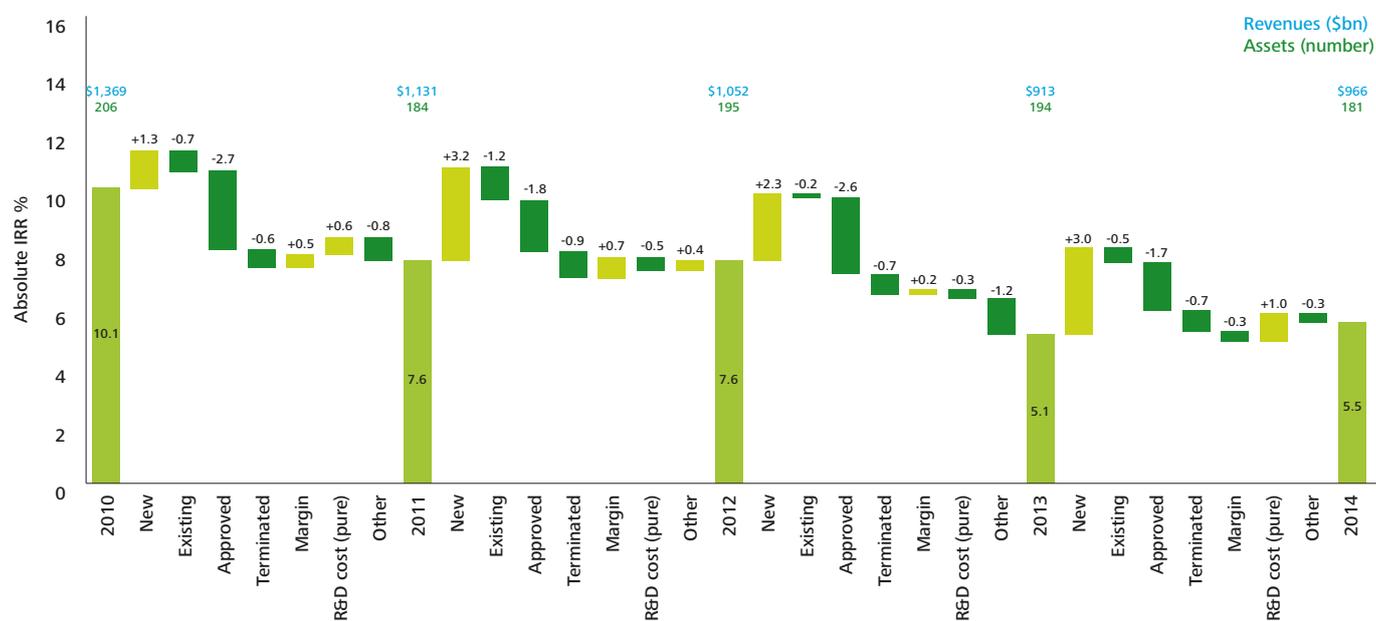
- some improvement has been made in maintaining forecast asset sales as they progress through the final phases of development
- no progress has been made in reducing the impact of late stage terminations

- improvements in operating margin were achieved each year between 2010 and 2013; however in 2014 operating margin exerted a small negative impact on returns.

Since 2010, the overall number of assets in the cohort's combined late stage pipelines has declined marginally, by 12 per cent. Over the same time period, projected total lifetime revenues have plummeted by almost 30 per cent, from \$1,369 billion to \$966 billion. Compared with 2013, our 2014 results show that this trend seems to be reversing: the total number of assets has continued to decline slowly while the projected lifetime revenues of those assets have increased. For the first time since 2010 the average forecast revenues of an individual asset have increased, almost making up the ground lost since 2012.

Since 2010, the overall number of assets in the cohort's combined late stage pipelines has declined marginally, by 12 per cent. Over the same time period, projected total revenues have plummeted by almost 30 per cent.

Figure 3. Drivers of change in IRR 2010–11, 2011–12, 2012–13 and 2013–14



Source: Deloitte LLP  
Other comprises phasing, licensing costs and tax rates.

# Part 2: Leading R&D organisations

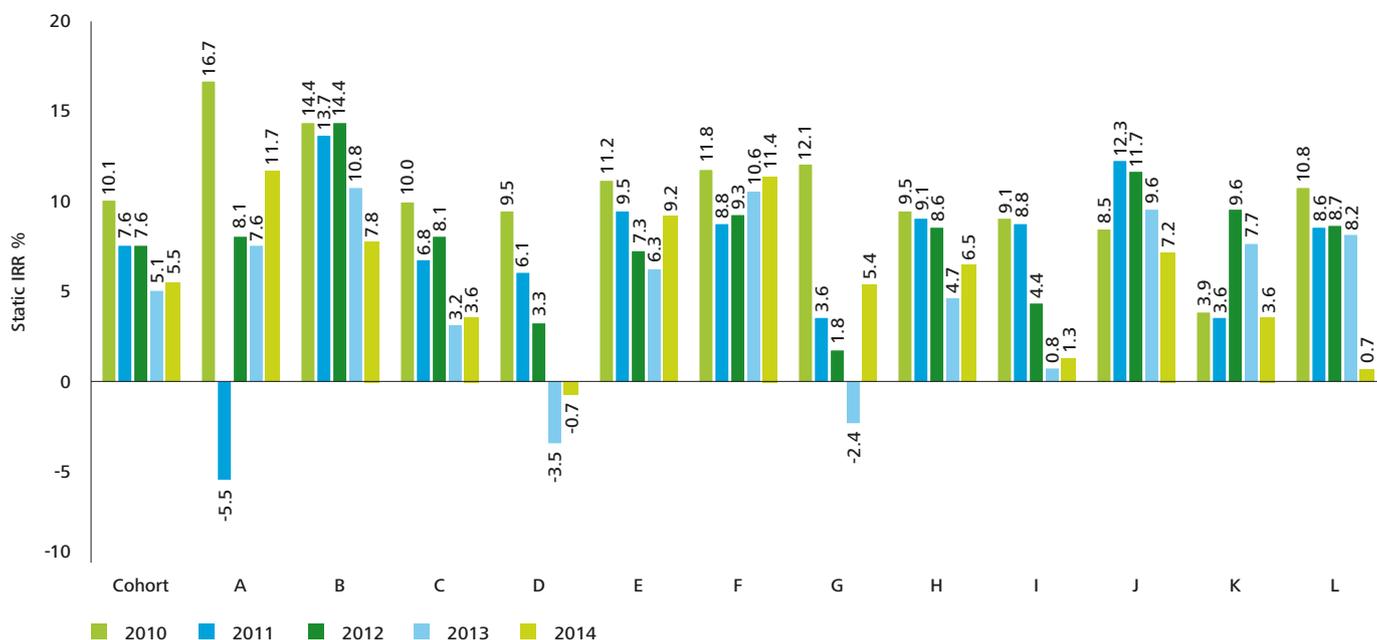
## At a company level there is wide variation in performance

In line with prior years, individual company performance over a single year varies widely across the cohort, with 2014 static IRR values ranging from -0.7 per cent (Company D) to 11.7 per cent (Company A) (see Figure 4).

The remainder of the analyses in this report focus on weighted three-year rolling average values and dynamic measures of IRR, which track drivers of R&D performance over time. As an asset typically spends just over three-years progressing through the late stage pipeline, a three-year rolling average removes the volatility associated with a yearly returns calculation and is, in our view, a more robust assessment of an organisation's long-term R&D performance.

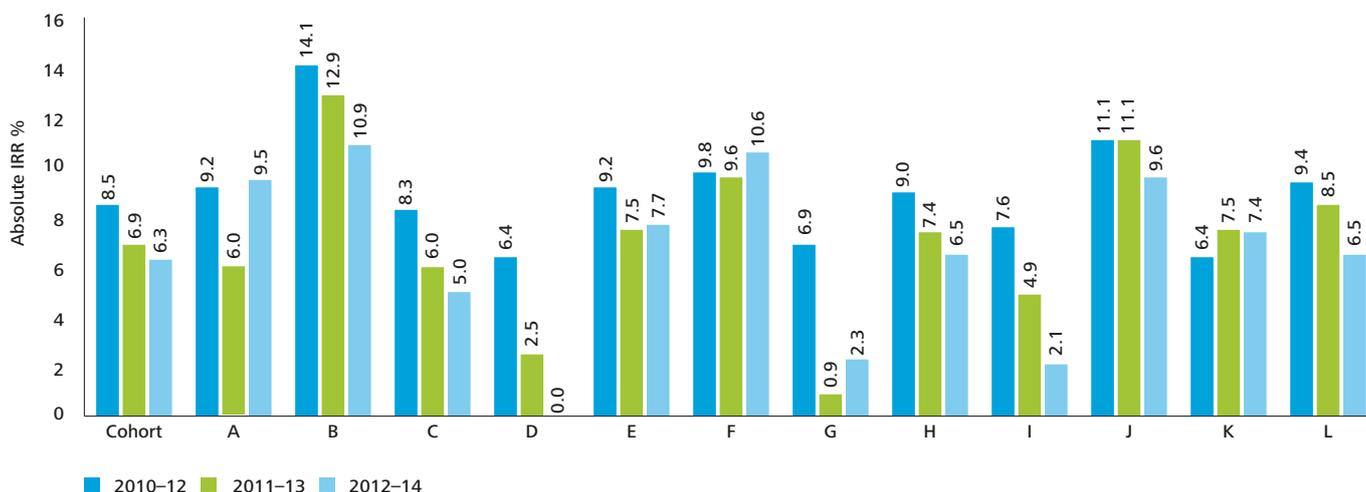
The three-year rolling average returns for the cohort have declined since 2010-12; however, there is still wide variation in company performance across the cohort (see Figure 5). Some companies (Company A, B, E, F and J) have remained particularly resilient in terms of maintaining a healthy level of predicted R&D returns, while for others (Company D, G and I) predicted returns have declined materially.

Figure 4. Comparison of static IRR results by company, 2010-14



Source: Deloitte LLP

Figure 5. Three-year average return on late stage portfolio, 2010–12, 2011–13 and 2012–14



Source: Deloitte LLP

### Pipeline momentum is an important measure of R&D returns success

Pipeline momentum analysis, the movement of assets into and out of the late stage pipeline and the impact this has on a company’s IRR (see Figure 6 and Figure 7), is explored using two composite measures:

- pipeline replenishment – the combined impact on IRR of changes to forecast revenues for existing assets as they progress through the late stage pipeline, along with revenue increases due to new assets entering the late stage pipeline
- net commercialisation – the impact on IRR of assets that are approved (as a positive), offset against any value lost due to terminations.

Companies that effectively balance net commercialisation with pipeline replenishment will be positioned in the top right hand quadrant of the pipeline momentum matrix (see Figure 7). These companies are sustaining a flow of new assets into the late stage pipeline and retaining or adding value to assets as they progress through the final stages of development. The impact of existing and new assets on IRR is sufficient to offset transfer of value out of the pipeline due to launches and loss of value due to terminations.

The five-year cumulative pipeline momentum view starts to separate out those companies that are outperforming their peers (see Figure 8). On a positive note, 11 of the 12 companies are located in the top-right quadrant of the pipeline momentum matrix, indicating that over the five-year timeframe, the majority of companies managed to balance late stage pipeline replenishment with successful commercialisation to some extent. However, some companies are clearly segmented from their peers:

- companies that are struggling to replenish their pipelines to balance their commercialisation success (Company L)
- companies that have optimised the balance between pipeline replenishment and commercialisation (Companies A, B, G, F, H and K) and a subset (Companies C, D and I) that need to deliver a slight improvement in pipeline replenishment to balance their successful commercialisation activity
- companies struggling to achieve commercialisation success, but that are innovating successfully (Companies J and E).

Figure 6. Drivers of late stage pipeline momentum

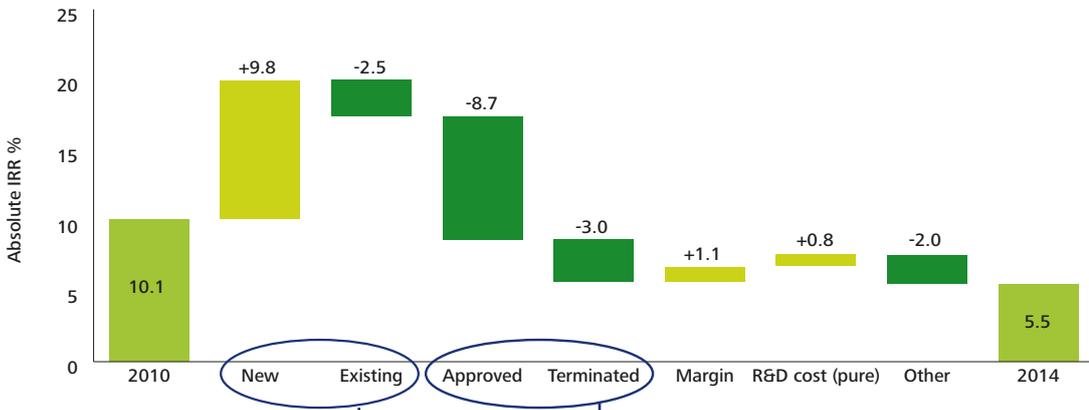
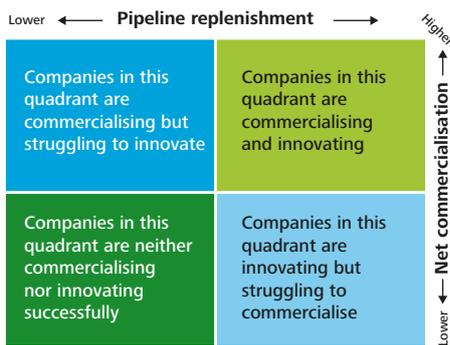
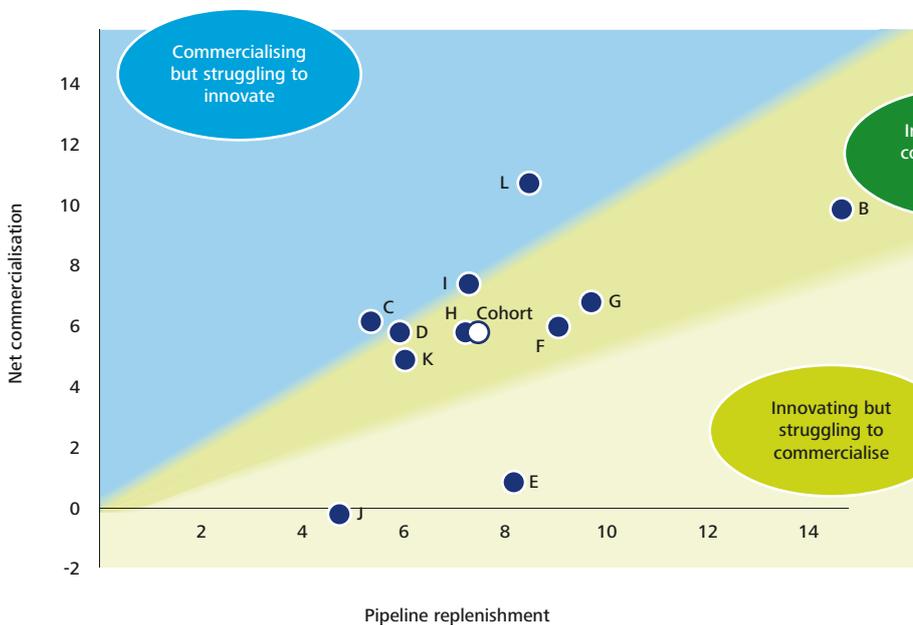


Figure 7. Pipeline momentum matrix



The five year cumulative pipeline momentum view starts to separate out those companies that are outperforming their peers.

Figure 8. Pipeline momentum performance, 2010–14



Optimal combination of pipeline replenishment and commercialisation ensures that sufficient value is being brought into the late stage pipeline to offset the transfer of value out, but is also sufficient to offset losses due to adverse changes in R&D cost, operating margin, licensing and tax rates.

Company A not shown to scale.

Source: Deloitte LLP research

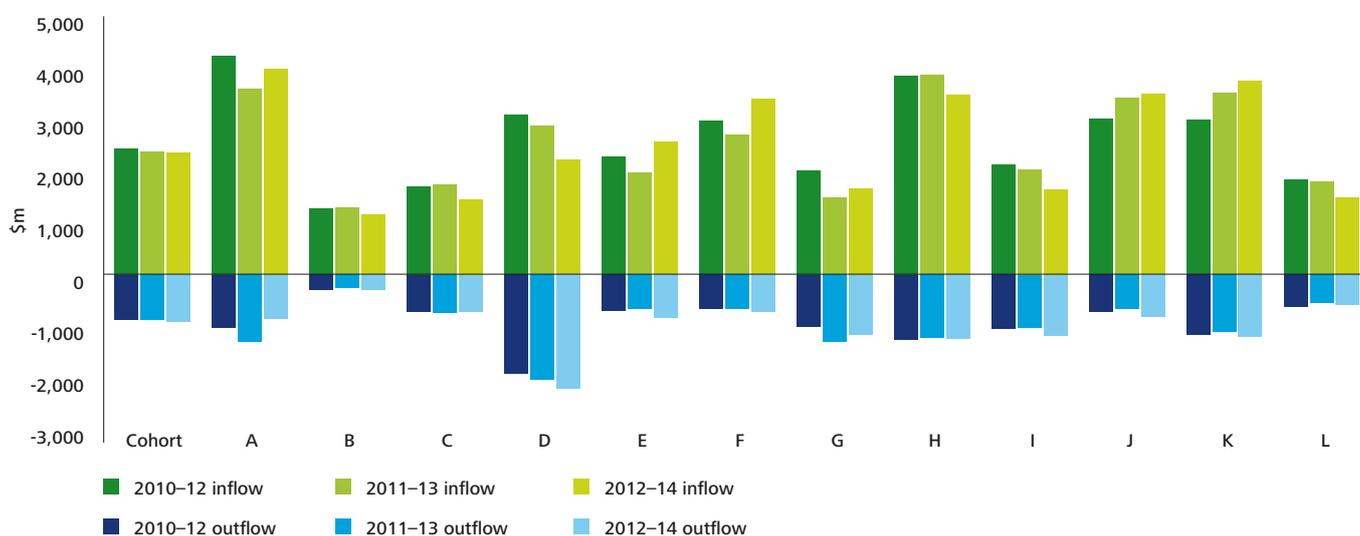
### The balance between cash outflows and cash inflows needs to be restored

As the costs of development increase, revenues (explored via three-year rolling cash inflows) are declining (see Figure 9). The balance between cash outflows and cash inflows per asset continues to be eroded, putting further pressure on R&D returns.

### The cost of bringing a product to market continues to increase

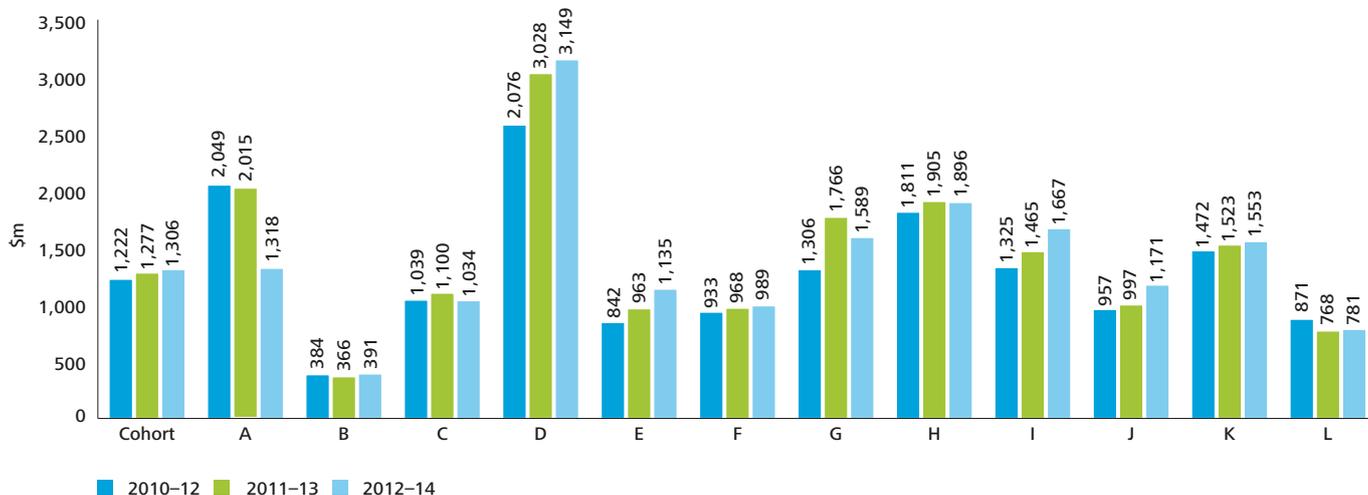
Across the cohort the cost of developing an asset (using three-year rolling averages) has increased by seven per cent (see Figure 10). Again, while there is wide variation in company performance, only a minority of companies (Company A and L) have realised any improvement in cost per asset since 2010.

Figure 9. Three-year rolling average outflow and inflow per late stage pipeline asset, 2010-14



Source: Deloitte LLP

Figure 10. Three-year rolling average R&D cost to develop an asset from discovery to launch, 2010-14



Source: Deloitte LLP

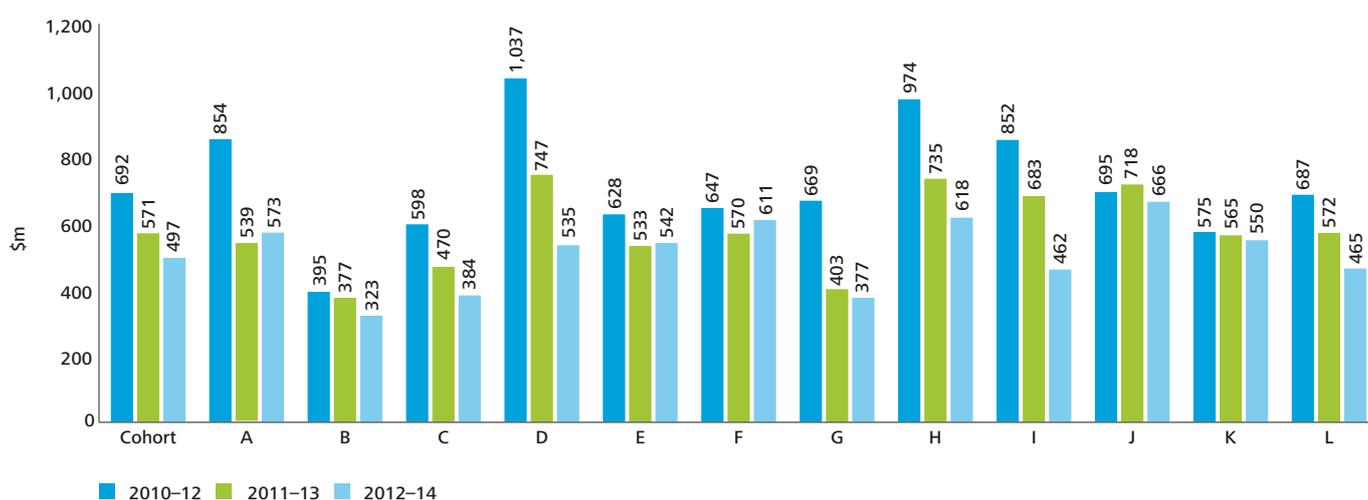
**Life sciences companies need to work more creatively to reduce the value lost through terminations**

Average cost per asset takes into account failed assets that have been terminated prior to Phase III or that do not successfully progress to the commercial portfolio. Since 2010 the cohort of companies has made little, if any, inroads into reducing the impact of late stage failures on R&D returns. It may be that there is a natural level of late stage terminations, but companies should consider whether there are ways to reduce the costs, identify the failures earlier or otherwise reduce the burden on R&D returns.

Clearly the ability to replenish R&D pipelines with innovative assets is fundamental to R&D returns success. Part 3 of this report explores the sources of innovation that the cohort is accessing to fill their late stage pipelines, along with other strategies being used to transform R&D returns.

Companies with smaller pipelines and fewer assets in development have less appetite to terminate, as terminating one asset in a small pipeline could have a significant impact on returns. However, for larger companies with a larger number of assets in development, trade-offs need to be made; the most promising assets need to be selected and resources focused on these assets. The question may not be: can late stage failure be reduced, but how can late stage failures be managed better. Are opportunities being missed to out-license, co-develop, repurpose or sell the less promising compounds to smaller organisations that would be able to focus all of their, albeit limited, resources on one asset. The importance of collaboration, networking and partnership within the life sciences industry is likely to be an important differentiator. Companies that are able to tap into a network of R&D partnerships and harness 'scientific crowdsourcing' will likely drive better returns as assets can be redirected through an alternative development route with different R&D partners within the innovation ecosystem.

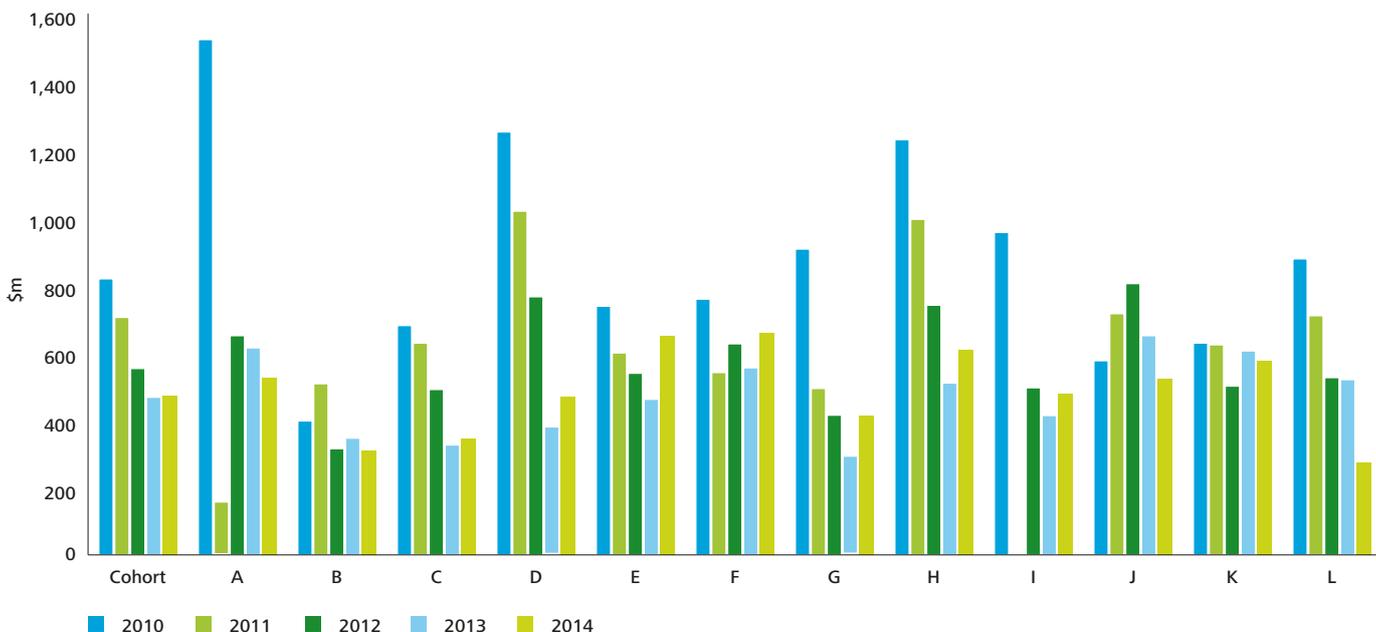
**Figure 11. Three-year rolling average peak sales per late stage pipeline asset, 2010–14**



Source: Deloitte LLP

The question may not be: can late stage failure be reduced, but how can late stage failures be managed better.

Figure 12. Average peak sales per asset, 2010–14



Source: Deloitte LLP

**Average peak sales per asset have declined significantly**

Forecast peak sales per late stage pipeline asset provide a direct measurement of how forecast asset value and late stage pipeline value have changed over time. A drop in asset sales will have a negative impact on R&D returns. Since 2010, average peak sales (three-year rolling average) across the cohort has declined by 28 per cent (see Figure 11). Although all the companies in our cohort have seen their average peak sales per late stage asset decline since 2010, our 2014 analysis shows a reversal of this trend. Average peak sales forecast per asset increased by \$5 million, with seven companies exhibiting an increase since 2013 (see Figure 12).

Clearly the ability to replenish R&D pipelines with innovative assets is fundamental to R&D returns success. Part 3 of this report explores the sources of innovation that the cohort is accessing to fill their late stage pipelines, along with other strategies being used to transform R&D returns.

Since 2010, average peak sales (three-year rolling average) across the cohort has declined by 28 per cent.

# Part 3: Drivers of R&D outperformance

There are four underlying 'levers' that improve R&D returns: increase product revenue, reduce R&D unit costs, reduce R&D cycle times and improve operating margins. These levers do not operate in isolation and a change in one lever is likely to have an impact on others. This section assesses some hypotheses for R&D outperformance by identifying certain characteristics of leading R&D organisations and how these characteristics influence the technical levers of R&D returns. The hypotheses we explore are:

- company size
- externalisation
- therapy area focus.

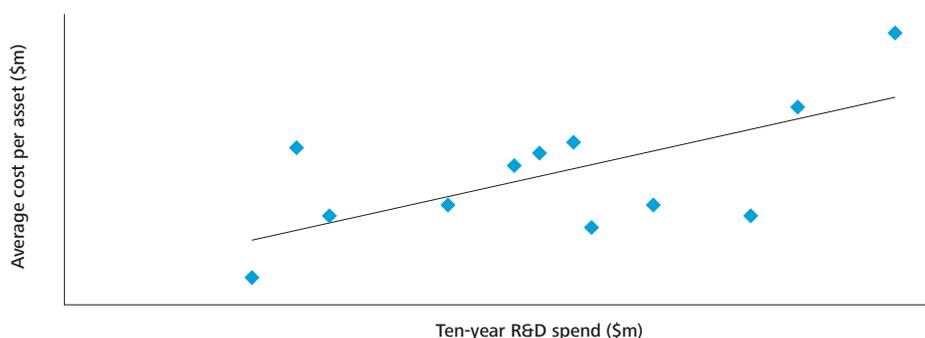
## Smaller companies appear to be developing assets more cost effectively and with better returns

Our analyses show that larger companies (according to level of R&D spend) are spending more per late stage asset than smaller organisations (see Figure 13). Smaller companies, as measured by both revenue and R&D spend, appear to be generating higher returns on their late stage portfolios (see Figure 14).

Those elements that contribute to the enhanced success of smaller companies need to be identified and applied in larger organisations so that scale can be adapted to work as an advantage. There are a number of smaller company characteristics that could be contributing to their success including less of a large organisational legacy and simpler system and data interoperability, which have an impact on both internal and external agility.

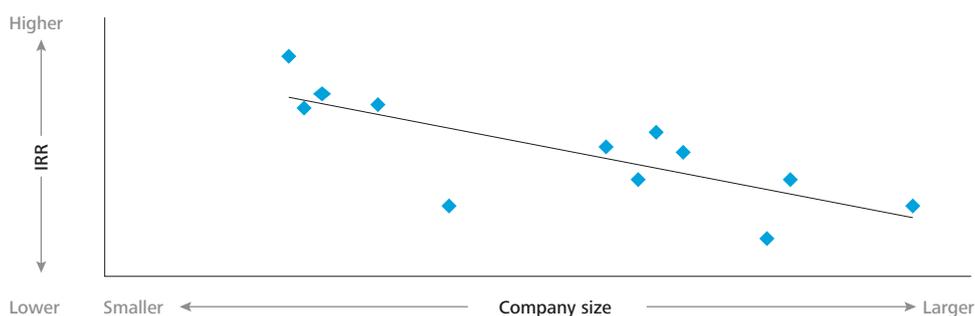
Larger organisations would likely benefit from initiatives to simplify operating models and improve their ability to collaborate, to prioritise and accelerate development times. It is notable that some large pharmaceutical companies have already begun to simplify operations and to establish groups in R&D with their own budget and relative autonomy. There are numerous examples of smaller groups operating autonomously within big pharmaceutical companies as a result of both internal restructuring and acquisition. The key characteristics of smaller R&D organisations which may be driving their success are; greater flexibility, more rapid and independent decision-making and focussing of resources.

Figure 13. Five-year weighted cost per asset vs ten-year R&D spend



Source: Deloitte LLP

Figure 14. Cohort company size vs weighted average five-year IRR



Source: Deloitte LLP

To protect the anonymity of the companies being analysed, units are omitted on the company size axis

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## Programme-driven, or variable R&D costs represent a significant opportunity to control R&D expenses.

Leadership skills are increasingly recognised as a key driver of R&D productivity, particularly given the changing nature of research. The advent of team based research, flatter organisational structures, more agile research models and the increasing need to work with multiple organisations have changed the nature of research leadership. Core skills in science need to be augmented with the ability to manage diverse groups, create compelling visions and build effective collaboration. While there is no single model of leadership that works across all research situations, we have seen research leaders increasingly benefit from exposure to leadership styles from other sectors.

### **Fixed and variable R&D costs can be managed more effectively**

Cost is not the largest driver of R&D IRR, but it is the lever that R&D organisations frequently pull to try and improve performance. Tactics such as site rationalisation and outsourcing have become commonplace in the industry. Each of these tactics can provide large life science R&D organisations with \$25 million to \$50 million in savings (operating expense) per year. However, organisations may not always look beyond infrastructure and headcount reduction measures and consider a wider set of cost reduction opportunities.

Programme-driven, or variable R&D costs represent a significant opportunity to control R&D expenses. Clinical trial costs have risen sharply: between 2000–03 and 2008–11, the median procedures per protocol increased by 57 per cent. Portfolio-wide efforts to minimise unnecessary procedures can provide annual savings that are equal to or even exceed those mentioned above.<sup>5</sup> More rigorous portfolio management and phase progression criteria can prevent investments in later phase studies for fringe assets that are more likely to fail. There are two challenges with facilitating these types of cost reductions:

- infrastructure or headcount related cost reductions tend to be aligned to organisational or functional leadership, whereas budgeting for programme and variable based costs are commonly granted on a programme-by-programme basis
- R&D operations groups are traditionally responsible for reducing costs, but variable-based expenses are controlled by TAs.

Managing and reducing R&D costs successfully requires a holistic strategy with an operating model that aligns these incentives and decision-making processes across the organisation.

### **Forecast revenues from externally sourced assets exceed those from internally generated assets**

In a modern R&D organisation, effective collaboration is seen as vital to successful innovation. The continued proliferation of strategic alliances, development arrangements, licensing deals, merger and acquisition (M&A) activity, and recent asset swaps exemplifies the industry's macro shift from creating innovation internally to accessing innovation externally. This shift has implications for R&D investment, operating models, talent and leadership development, and portfolio governance.

### **External innovation accounts for the majority of forecast late stage pipeline value**

The proportion of late stage pipeline revenues relating to externally acquired science and innovation (via acquisition, co-development/joint venture or licensing) was analysed across the cohort and by company using the risk adjusted peak sales forecast for each asset (see Figure 15 and Figure 16). Externally generated assets are forecast to deliver 58 per cent of late stage pipeline revenue in 2014; 59 per cent of new molecular entity (NME)/new biological entity (NBE) valuation if line extensions are excluded.

This is the fifth consecutive year that externally generated assets are forecast to deliver the majority of the cohort's late stage pipeline revenue, although there is a significant difference between companies, ranging from 35 to 85 per cent of pipeline revenue.

In 2014, nine of the 12 companies in the cohort had forecast late stage pipeline revenue that was predominantly externally driven (see Figure 16).

This external contribution has been stable over the past five years, suggesting that investing in capabilities to support sourcing and executing agreements with external collaborators as part of the R&D organisation will be critical for the cohort of companies to replenish their late stage pipelines. Indeed, externalisation has been successful in relieving both profit and loss pressure and mitigating R&D risk through variable deal structures and option clauses that allow partners to exit deals early.

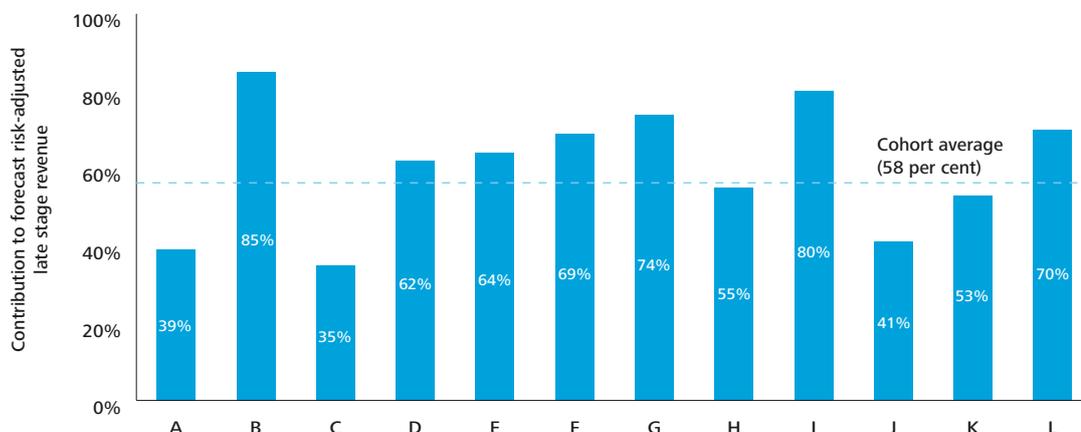
Externally generated assets are forecast to deliver 58 per cent of late stage pipeline revenue in 2014.

Figure 15. Sources of cohort late stage pipeline revenue, 2014



Source: Deloitte LLP  
2010-14 risk-adjusted peak sales projections of company late stage pipelines

Figure 16. External component of individual company late stage pipeline revenue, 2014



Source: Deloitte LLP

The mean risk-adjusted peak sales of assets with breakthrough designation are 20 per cent higher when sourced externally, and for orphan drugs the figure is 54 per cent higher.

**Highly innovative externally sourced assets deliver higher projected revenues than their internal counterparts**

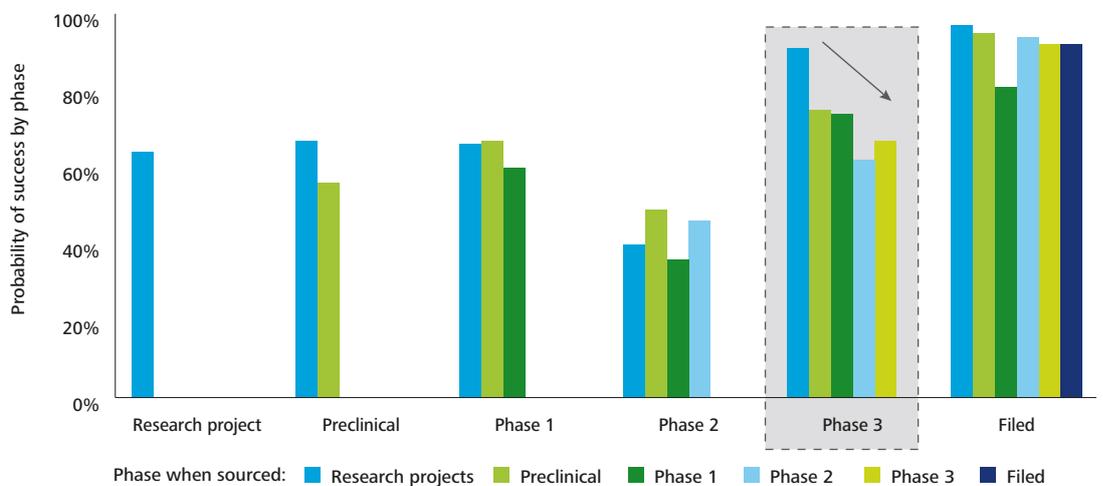
Our analysis of the 2014 data shows that at the cohort level the mean risk-adjusted peak sales potential of externally sourced assets is six per cent higher than internally generated assets. For highly innovative assets or those that fulfil areas of unmet need, the difference between internally and externally sourced assets is even greater. The mean risk-adjusted peak sales of assets with breakthrough designation are 20 per cent higher when sourced externally, and for orphan drugs the figure is 54 per cent higher.

To date, our analysis does not show a correlation between level of external innovation and R&D returns at a company/portfolio level.

**The optimal time for sourcing external assets is early in the R&D lifecycle**

Our analysis indicates a ‘sweet spot’ or optimal point in the development lifecycle for sourcing external assets. There is a strong correlation between early licensing and value, with assets acquired in the early stages of development more likely to progress to later stages of development than those sourced in their current phase of development (see Figure 17). For example, assets sourced during research, preclinical and Phase I performed better in Phase III trials than assets sourced in Phase III. This infers there is a benefit in licensing earlier to control or own clinical studies to minimise execution risk; alternatively, late stage deals may be overly optimistic when evaluating late stage success rates.

**Figure 17. Phase transition probabilities of externally sourced assets, 1990–2014**



Source: Deloitte Consulting LLP; Evaluate Pharma Database. Includes assets sourced between 1990–2014 for the 12 largest biopharmaceutical companies, and excludes OTCs, Generics and Biosimilars. Note: In-licensed assets later acquired via company acquisition are treated as in-licensed assets for the purpose of this analysis.

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## Early stage deals can provide long-term value and help companies generate long-term revenues, but this does not address short-term pressure to deliver revenue targets and fill late stage pipeline gaps.

Our analysis indicates that assets acquired early in the development lifecycle, preclinical or Phase I depending on drug type and TA, are more durable than those acquired at later stages of development. There are several reasons for this including:

- preclinical and Phase I assets, while still at an earlier stage, are partially derisked
- early stage deals offer a more favourable structure – reduced upfront fees and downstream fees that are more heavily contingent on commercial success
- sourcing at earlier stages affords more input into the asset's overall development programme, for example indications and clinical trial protocols, that may decrease execution risk and increase commercial value
- late stage deals typically command a significant price premium.

There are two notable challenges with early stage external sourcing – timing and valuation. For timing, most organisations have made strategic choices to increase their emphasis on early stage sourcing, but discipline and adherence to these strategies are challenging. Early stage deals can provide long-term value and help companies generate long-term revenues, but this does not address short-term pressure to deliver revenue targets and fill late stage pipeline gaps. Valuing early stage deals is difficult as companies typically rely on methods more appropriate for late stage deal measurement, such as net present value (NPV).

Mid- to large-scale M&A is often the solution to corporate challenges including filling R&D pipelines, but this is rarely an R&D investment which adds value in the long term. These transactions are disruptive to organisations and often require significant price premiums. Deloitte's analysis of three of the cohort's mega-mergers in the last five years indicates that of the \$140 billion in transaction value, \$32 billion (23 per cent) was associated with goodwill. Moreover, \$25 billion (17 per cent) was attributed to in-process R&D which effectively corresponds to an additional 23 per cent of the combined organisation's R&D expenses. The level of returns realised from an R&D perspective have not justified this level of outlay.

A sound external innovation strategy can help organisations manage continuous pipeline flow and achieve both short- and long-term revenue/growth targets. It can also support portfolio management approaches when there is a need to fill a pipeline gap due to a paucity of internally-developed assets.

As well as being attractive to large pharmaceutical companies to source innovation (assets and capabilities) over the last decade, biotechnology companies have exerted a disruptive influence on the life science industry's strategies, investments and operating models. In responding to the impact of disruptive technologies, the life science industry can learn from the experiences of other industries, as highlighted overleaf.

## Using external sources of innovation to access disruptive technologies

Commentary by Julian Birkinshaw, Professor at London Business School and Director of the Deloitte Institute of Innovation and Entrepreneurship.



Harnessing the potential of biotechnology has been a major strategic imperative for large pharmaceutical companies over the last decade. The biotechnology revolution does not just require large companies to refocus around new technology areas; it also demands new ways of working, especially in terms of sourcing ideas and capabilities from outside. To figure out how best to respond, it is useful to draw lessons from other industries that have been shaken up by disruptive technologies. Based on the research my colleagues and I have been undertaking over the last ten years, there are some important principles here that can be directly applied to the life sciences industry.

- 1. Separate then integrate.** The media companies that coped best with digitisation, such as The New York Times, created separate digital units at first, reporting in at a very high level and protected from the traditional print businesses. As soon as there was customer uptake, they were reintegrated and pushed to work collaboratively with the traditional platforms. What does this mean for pharmaceutical companies? Most have gone through the separation phase already; the challenge now is to achieve a comprehensive integration of the 'old' and 'new' models across the entire value chain.
- 2. New technologies need new ways of working.** Whenever a disruptive technology emerges, it takes a while for new patterns of consumer behaviour and new ways of working to catch up. We used to print out images from our digital cameras, now we upload them to Instagram. Newspapers used to post simple text online, now they create integrated video/text/graphic content. Following on from the previous point, it is not enough for pharmaceutical companies just to integrate their biotechnology activities with their traditional ones – they need to rethink what customers are actually buying, and how they can be served better. Biotechnology companies are typically better at cross-functional collaboration than traditional big pharmaceutical companies and they tend to work more closely with users.
- 3. Collaboration takes a long time to get right.** In the late 1990s, Lego built partnerships with technology providers, as a logical first step in embracing the world of screen-based games. But their early game and video offerings were poor quality, their brand suffered and they lost focus. A decade later, Lego is thriving again by refocusing on its core market, and by (eventually) building the internal capabilities it needed to work with gaming and media companies. The recent Lego Movie is a perfect blend of their old and new capabilities. What is the lesson here for pharmaceutical companies? First, you cannot just buy or partner your way out of trouble – it takes years to build the deep knowledge to succeed with novel disruptive technologies. Second, do not lose sight of your core business – as with Lego, it is not completely disappearing, so make sure to stay on top of it.
- 4. Awareness is good, commitment is better.** Kodak invented the digital camera in 1975 and had invested \$5 billion in digital technologies by 1993. So they did not actually miss the digital revolution at all. But throughout the 1980s and 1990s they adopted a 'scattergun' approach, trying out a range of digital products and technologies, but never putting their full weight behind any of them. Customers ended up confused and employees didn't know where to focus their efforts. The lesson here? As leaders, you need to seek out the inflection point (which for Kodak was in the late 1990s) and then be prepared to move decisively to the new technology. Intel's leaders famously did this when they shifted the company from memory chips to microprocessors in the early 1990s. Many big pharmaceutical companies are in the midst of such a transition. In such circumstances, decisive leadership pays big dividends.

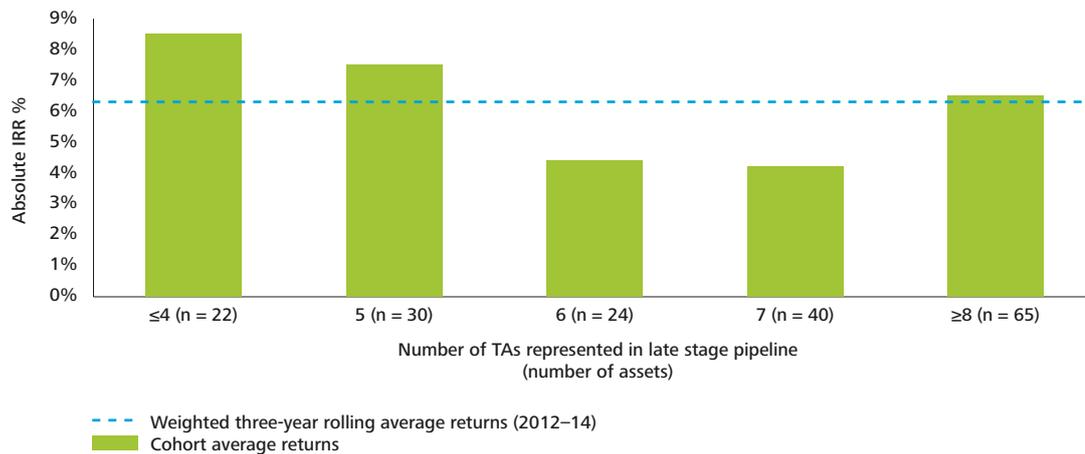
*Professor Birkinshaw is a leading authority on innovation in large established companies. He was ranked #39 in the 2013 "Thinkers 50" list of management gurus, and was listed among the top 100 Economics and Business academics in the 2014 "World's Most Influential Scientific Minds". He has written 12 books and over 80 articles in journals such as the Harvard Business Review and consults with a wide range of industries ranging from pharmaceuticals, financial services, media, mining and engineering.*

**Therapy area focus delivers commercial advantage**

Our analysis identifies a correlation between stronger TA focus and late stage pipeline returns (see Figure 18). Companies that focus on less than four TAs are delivering higher returns than companies focused on five or more. This difference is more pronounced when companies are focussed on six or more. The commercial advantages of having a strong TA focus include:

- improved scientific knowledge of a disease or its underlying mechanisms
- a shift in emphasis from a product based view to a more comprehensive disease management based view
- the ability to use deep TA expertise with commercial payers when negotiating price, reimbursement and market access
- an aptitude to qualify and assess external innovation opportunities to acquire or develop jointly.

**Figure 18. Weighted three-year rolling average returns (2012–14) vs number of TAs in 2014 pipelines**



Source: Deloitte LLP

# Part 4: Conclusions

Since 2010, projected R&D returns have declined significantly, however, our 2014 analysis indicates that the cohort may have turned a corner and is starting to move in a positive direction. While the cost of bringing an asset to market continues to increase year-on-year and the detrimental impact of terminations remains unchanged, pull-through of new assets into late stage pipelines has provided welcome relief from the steady downward pressure. This bodes well for the cohort over the next few years.

Within our cohort company size appears to be inversely correlated with R&D returns, reinforcing the view that smaller, simpler, more dynamic and flexible R&D units that are empowered to make decisions are better equipped to survive the challenges faced by life science innovators today and in the future.

Life science innovation takes up to 15 years to realise returns. Externalisation strategies are typically used as a quick fix for filling short-term revenue and/or growth gaps. For companies seeking innovation externally, the driver is almost certainly the need to find high quality assets for the TA in which they have a particular interest or focus.

However, our analysis to date does not show a correlation between externalisation and R&D returns at either the company or portfolio level. Possessing the skills and capabilities to manage strategic partnerships and collaborate with life science innovators is fundamental to long-term R&D success; as is the ability to time and value external sources of innovation optimally.

The life sciences R&D ecosystem is undergoing a transformation that has forced the industry's biggest players to reinvent how they access, foster and commercialise innovation. Our analysis indicates that some of the top 12 organisations are further through the journey than others and, as a result, are delivering leading returns.

The majority of the industry's projected pipeline revenues are now coming from external sources of innovation and external assets are showing higher future sales forecasts than those developed internally. Companies need to consider if they have invested in capabilities that make them 'collaboration ready', including the talent, processes, infrastructure and data required to collaborate effectively for the long term without eroding the value acquired.

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... simpler, more dynamic and flexible R&D units that are empowered to make decisions are better equipped to survive the challenges faced by life science innovators today and in the future.

# Appendix: Methodology

Deloitte LLP has built an interactive model to calculate the Internal Rate of Return (IRR) for the companies and compounds of interest. This part of the report contains a top-level summary of the methodology. A detailed description can be found at: [www.deloitte.co.uk/measuringrndreturns2013](http://www.deloitte.co.uk/measuringrndreturns2013)

## Company cohort

The cohort has remained consistent since 2010 and comprises the top 12 publicly-listed, research-based life science companies measured by 2008-09 R&D spend: Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck & Co., Novartis, Pfizer, Roche, Sanofi and Takeda.

## Compounds evaluated

The analysis focuses on each company's late stage pipeline defined as the set of compounds that are in Phase III clinical development or submitted for approval as of 30 April for each relevant year. Given the increasing potential of compounds that have been given breakthrough therapy designation by the US Food and Drug Administration progressing straight from Phase II to submission, this year's report also includes compounds in Phase II with breakthrough therapy designation. The types of compound included are:

- new chemical entities (NCEs)
- new biological entities (NBEs)
- significant line extensions expected to result in a measurable uplift in revenues
- reformulations
- fixed dose combinations
- biosimilars.

For all compounds included in the analysis, their origin was assessed and they were categorised as self-originated, in-licensed, part of a joint venture/co-development or acquired.

## Methodology amendments

For the 2014 report Deloitte has partnered with GlobalData to provide forecast data.

To provide assurance that any observed trends could be attributed to individual company performance and not changes in the data forecasting methodology, a validation exercise was performed. This compared forecast revenues used in the 2013 report with revenues forecast for the same set of compounds, for the same time period, for a sample of companies. No material difference between the original and reforecast 2013 data was found.

For the 2014 analysis it was decided to adjust the timeframe over which average operating margins are calculated based on discussions with clients. This was primarily to ensure the impact of recent operational efficiency programmes was considered and to more closely reflect the economic environment into which the compounds are expected to launch. Historical results published in previous reports have been recalculated to allow for valid year-on-year comparisons. It is noted that, despite minor changes in the company and consolidated figures, the trends for all companies remain consistent with the data published originally.

## Principles applied to the model

### Currency

All calculations have been performed in US dollars. Financial Times yearly average rates have been used for conversion of other currencies into US dollars.

### Taxation

IRR has been calculated based on post tax inflows and outflows. Company specific tax rates have been calculated based on average effective tax rates over the ten years to 31 December 2010, 2011, 2012, 2013 or 2014, adjusted for non-recurring items, such as litigation costs, impairments and in-process R&D expense.

### IRR calculation

IRR is a measure which equates the cost of developing an investment and the expected benefits that the investment will deliver. The methodology assesses two IRR measures; static returns and dynamic returns.

#### Yearly, static returns

Calculated by equating cash outflows with cash inflows to generate an IRR value, with a separate IRR value generated for each year under investigation (see Figure 19).

Static returns is calculated for a defined basket of late stage compounds by estimating the expenses associated with developing the compounds and the likely potential returns that they will deliver. This is achieved using estimates of each company's:

- annual R&D expenses (cash outflows) for the prior ten years – which calculates the cost associated with bringing the basket of compounds to a particular stage of development

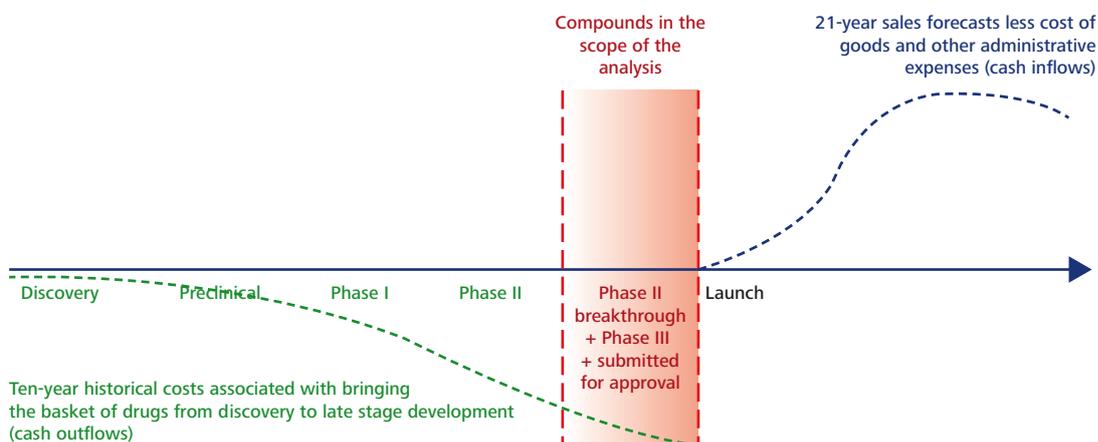
- annual risk adjusted revenues (cash inflows) forecast for the future 21 years – which estimates the likely returns that the basket of compounds will deliver.

#### Dynamic returns

Calculating the dynamic returns allows the movement in static returns from one year to the next to be reconciled and also quantifies the key elements driving this change (see Figure 20). It is calculated for four time periods; 2010–11, 2011–12, 2012–13 and 2013–14, and focuses on the same basket of late stage pipeline compounds as static returns. However, the basket of compounds changes year on year due to the movement of compounds into and out of the late stage pipeline.

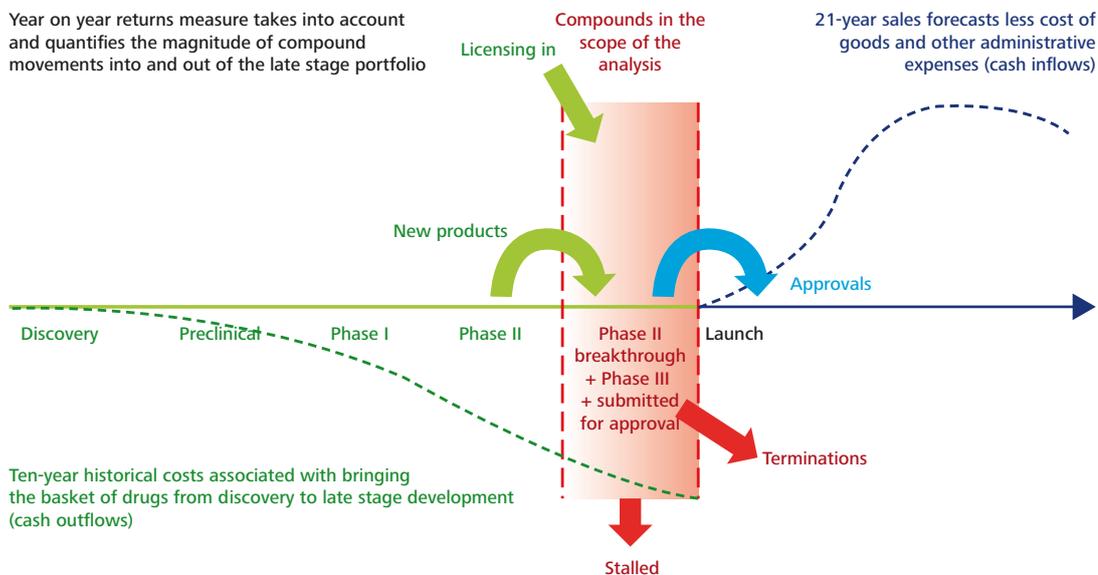
The elements driving change in IRR can be categorised into two groups, based on whether they impact cash outflows or cash inflows.

Figure 19. Calculating yearly, static returns



Source: Deloitte LLP

**Figure 20. Determining the drivers of year-on-year dynamic returns**



Source: Deloitte LLP

**Cash outflow elements**

The four outflow elements driving change in IRR comprise:

- R&D cost – changes to R&D costs for self-originated compounds
- cost phasing – changes to how R&D costs are allocated over the historical ten year time period
- licensing – increases or decreases in licensing expenses associated with the basket of compounds under review
- tax rates – alterations to the company specific tax rates based on average effective tax rates over the historical ten year period.

**Cash inflow elements**

The five inflow elements driving change in IRR comprise:

- terminated – future revenues lost from late stage pipeline due to termination of compounds
- approved – transfer of revenues to the commercial portfolio due to compounds leaving late stage pipeline and being launched
- existing – increases or decreases in forecast revenues for compounds which remain within the late stage pipeline
- new – revenues associated with new compounds entering the late stage pipeline
- margin – changes in a company’s average cash operating margin.

### Model inputs: R&D cash outflows

Cash outflows were calculated separately for self-originated, in-licensed and acquired compounds.

#### Self-originated compounds

1. R&D costs have been obtained from publicly available company reports results based on applicable GAAP at the time results were issued (either local GAAP applicable in the country of incorporation, IFRS or US GAAP).
2. R&D costs recognised through profit and loss accounts are assumed to equal cash flows, unless a non-cash expense is separately disclosed (e.g. write off of in-process R&D charge recorded under US GAAP) in which case this has been excluded from the R&D cost.
3. Following a business combination, R&D costs include those of the enlarged group, in line with the publicly available company reports (see below for pre-acquisition costs).
4. The use of publicly available data limited the model to the use of industry average cycle times and cost allocation when calculating R&D costs over the ten year period; GlobalData proprietary data was used for 2014 (see Table 1). This methodology incorporates the cost of attrition of compounds from the initial cohort at discovery to the late stage pipeline as at 1 January for each respective year.
5. R&D costs have not been included within the model beyond 31 December 2013.

#### Compounds acquired through in-licensing

For compounds which have been in-licensed from a third party, any upfront payments have been included in the relevant year of acquisition. In-licensing information was provided by GlobalData. In most cases financial information was limited due to the commercial sensitivity of deal information. As publicly available data typically does not include the timing or quantum of future contingent payments, the total amount of these costs associated with the relevant in-licensed compound have been assumed to be incurred at their maximum potential amounts on commencement of sales of the compound. Any costs expended in developing the product subsequent to the in-licensing have been included as per the internally developed compounds.

Where deal values have not been disclosed, industry averages by therapy area have been utilised as a proxy for the costs of acquiring IP. Industry average royalty rates per stage of development at the time of deal formation have also been utilised.

For deals involving a basket of compounds, deal values have been weighted according to the number of compounds for deals done in early stage, or, for late stage deals where lifetime sales forecasts are available, weighted according to the revenue contribution from the individual constituents of the deal.

Table 1. Industry average benchmarks, 2014

2014 industry average benchmarks	R&D cost allocation	R&D cycle times
Discovery to first toxicity dose	27%	25%
Preclinical to Phase II	36%	29%
Phase III and submission	37%	46%

Source: GlobalData proprietary data

### Compounds acquired as part of a business combination

R&D costs arising from compounds acquired as part of a business combination enacted by an entity have been included in the model if considered material to the calculation of IRR.

1. R&D costs incurred after the date of the business combination have been included as per the internally developed compounds noted above.
2. R&D costs incurred prior to the date of the business combination have been included separately in the model obtained from publicly available company reports based on applicable GAAP at the time results were issued (either local GAAP applicable in the country of incorporation, IFRS or US GAAP).

Private companies acquired were not considered as access to the required financial data is not widely available. The cost associated with the acquisition of a compound as part of a business combination has not been included as the acquired company's pre-acquisition R&D cost is included as per the internally developed compounds. Furthermore publicly available data does not typically include the fair value attributed to each of the compounds acquired. Any costs expended in developing the product subsequent to the business combination have been included as per the internally developed compounds.

### Model inputs: Forecast cash inflows

#### Revenue forecasts

1. Company revenues were forecast for a 21-year timeframe for each time period under investigation, for example, for 2014 models – revenues were forecast from 1 January 2014 – 31 December 2034.
2. 2014 revenue forecasts were calculated by GlobalData using a combination of forecasting methodologies, including analyst consensus forecasts and proprietary patient-based forecasting models to generate revenues to 2034.
3. Revenue forecasts have been risk adjusted for Phase III and submission success rates specific to therapeutic areas (GlobalData proprietary data).
4. Sales forecasts were determined in July 2014; forecasted revenues are accurate as of this date.

5. After reaching peak sales, standard erosion curves were applied depending on the type of compound considered. Different erosion curves have been developed for each compound type; small molecules (chemical entities) and large molecules (biological entities).
6. Available patent information was extracted by GlobalData from GlobalData's Pharma eTrack and other public patent sources for each compound. Accurate patent data can be difficult to locate therefore a number of rules were defined to ensure consistency across the compounds.

#### Margin applied to forecast revenues

Inflows have been determined by applying an average cash operating margin. This has been calculated using operating profits reported in publicly available company reports over the three years preceding each year, 2010, 2011, 2012, 2013 and 2014.

#### Modelling assumptions

The use of revenue forecast data and publicly available information regarding pipelines and deal information presents certain challenges and risks associated with the construction of revenue forecasts and distribution of R&D costs within the life sciences industry. These challenges and risks are summarised in the detailed methodology which can be found at: [www.deloitte.co.uk/measuringrndreturns2013](http://www.deloitte.co.uk/measuringrndreturns2013)

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# Notes

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