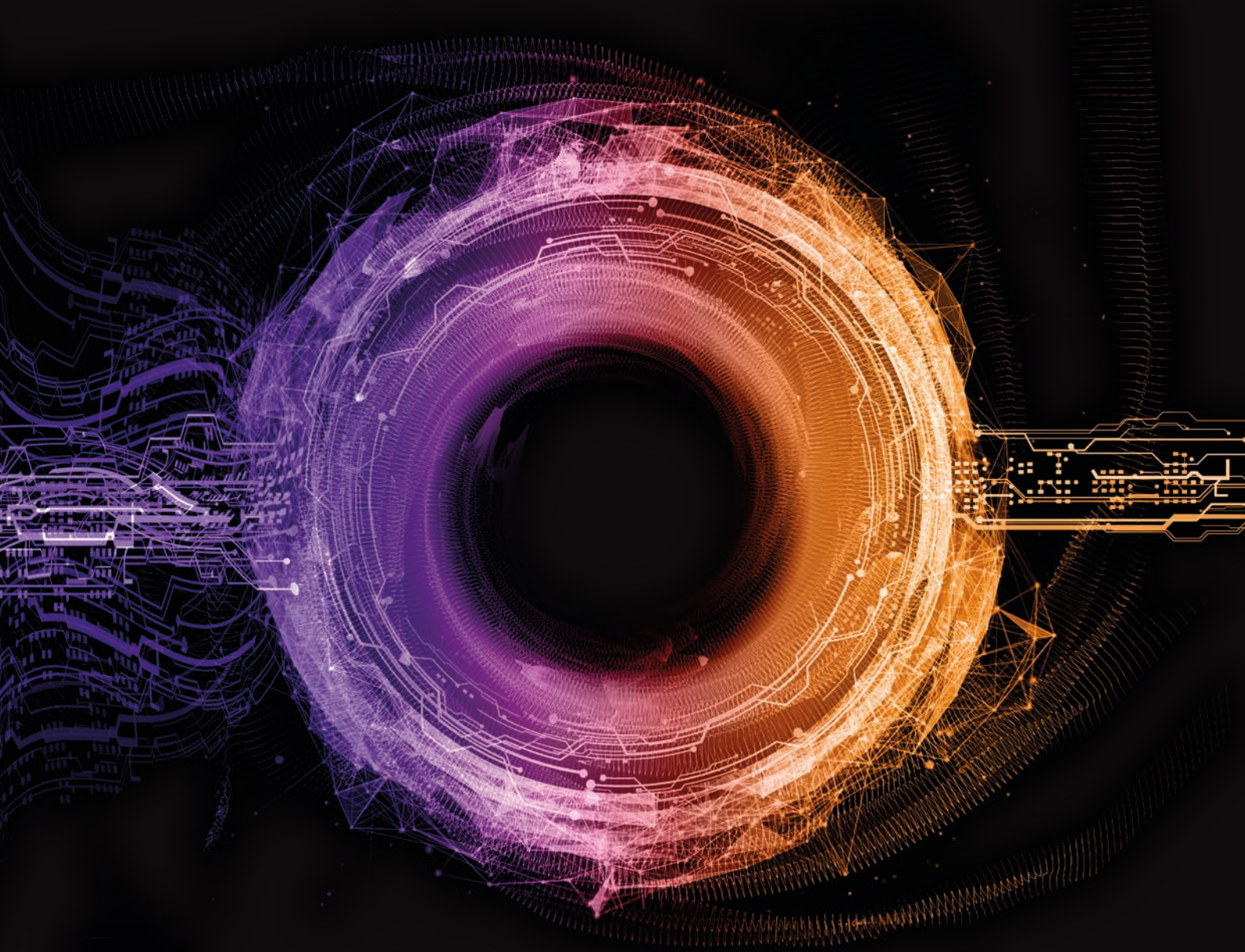


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Health Solutions



**Measuring the return from
pharmaceutical innovation 2017**
Methodology

 **GlobalData.**

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Deloitte Centre *for* Health Solutions

The Deloitte Centre for Health Solutions

The Deloitte Centre for Health Solutions is the research arm of Deloitte LLP's Life Sciences and Health Care practices. Our goal is to identify emerging trends, challenges, opportunities and examples of good practice, based on primary and secondary research and rigorous analysis.

The UK Centre's team of researchers, working in partnership with colleagues from the US Center for Health Solutions, seeks to be a trusted source of relevant, timely and reliable insights that encourage collaboration across the health value chain, connecting the public and private sectors, health providers and purchasers, patients and suppliers. Our aim is to bring you unique perspectives to support you in the role you play in driving better health outcomes, sustaining a strong health economy and enhancing the reputation of our industry.

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GlobalData.

GlobalData

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.

Introduction

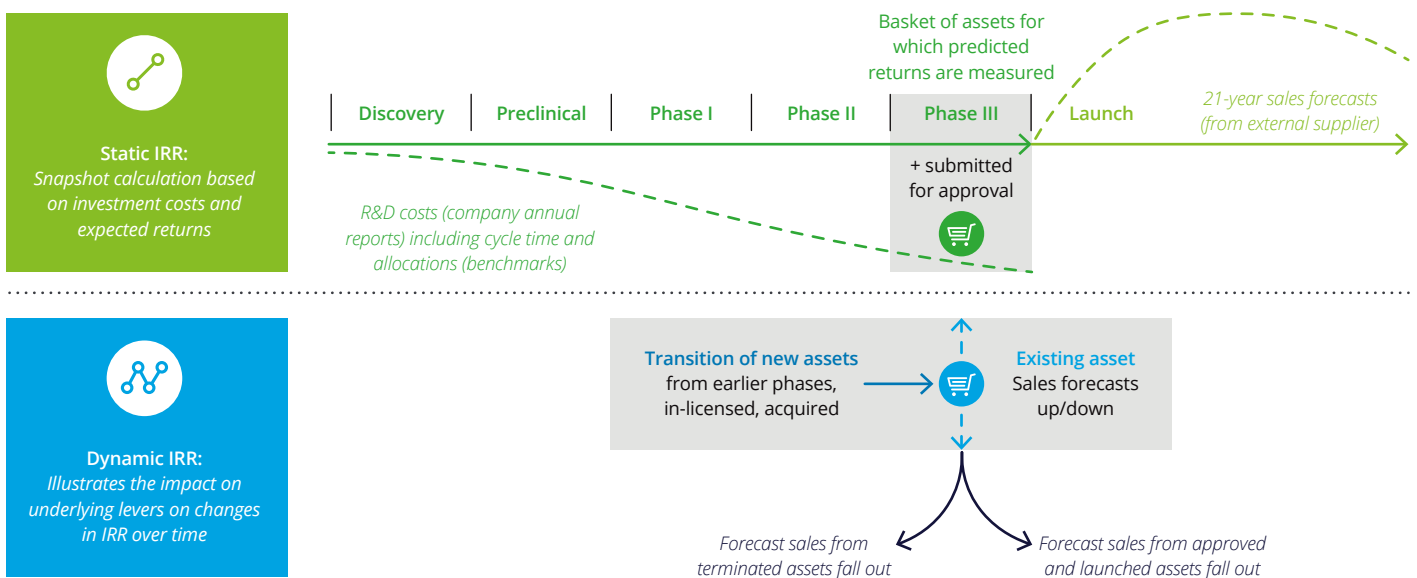
Deloitte's annual report 'Measuring the return from pharmaceutical innovation', published since 2010, provides estimates of the return on investment that 12 leading biopharma companies might expect to achieve from their late-stage pipeline of assets. Since 2015 the analysis has also included an extension cohort of four mid-to-large cap biopharma companies allowing us to compare and contrast their performance against the original cohort.

Our analysis is focused on assets that are currently in late-stage development and expected to launch within the next one to four years, using data from publicly available audited annual reports and forecasts provided by GlobalData. This document provides an overview of the methodology applied.

Methodology

Deloitte LLP has built an interactive model to calculate the Internal Rate of Return (IRR) for the companies and late-stage assets of interest. Whilst we acknowledge measuring projected returns is complex and therefore imperfect, the analysis that underpins our series of reports aims to provide a consistent and objective measure of industry performance. In turn this allows us to derive insights into opportunities for improving return on investment in R&D. The underlying principles we have applied are comparability (a consistent, unbiased, direct comparison across the industry and investments of different sizes), accessibility (relevant to a diverse audience, both within and outside of the biopharma industry) and availability (the analysis is derived from publicly available information available in audited annual reports or is readily accessible from third-party data providers). A high-level overview is provided by Figure 1.

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



Source: Deloitte research, 2017

Original cohort

The cohort has remained consistent since 2010 and comprises the top 12 publicly-listed, research-based life sciences 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.

Extension cohort

The extension cohort have been selected based on perceived recent performance and pharmaceutical R&D spend. All fall within the top 25 pharmaceutical companies based on R&D spend for 2012 to 2014: AbbVie, Biogen, Celgene and Gilead Sciences.

Assets evaluated

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

We are continually working to improve the methodology and modelling that underpins this report. Due to the complex nature of the analysis and despite rigorous quality review procedures errors are occasionally identified in previously published data.

Any methodology amendments are adjusted for retrospectively, allowing year-on-year comparison of trends. Where errors are identified, an assessment as to the materiality of the error is made based on the impact this has on IRR. Judgement is then applied to determine whether to amend results retrospectively. No adjustment is made where new information subsequently becomes available which was not available at the time of performing the analysis, for example, incorporation of actual sales data or restatement of figures published in company annual reports.

Principles applied to the model

Currency

All currency calculations have been made in US dollars. 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 preceding the year of the report, adjusted for non-recurring items, such as litigation costs, impairments and in-process R&D (IPR&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 three IRR measures: static returns, average 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 of the report.

Static returns are calculated for a defined basket of late-stage assets by estimating the expenses associated with developing the assets 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 assets 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 assets will deliver.

Average returns

Average returns are calculated on a weighted three-year rolling average basis by aligning the individual inflows and outflows used in the static returns figure for the three periods included in the rolling average.

Dynamic returns

Calculating 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. It is calculated to bridge each time period, as well as the overall time period from 2010, and focuses on the same basket of late-stage pipeline assets as static returns. However, the basket of assets changes year-on-year due to the movement of assets 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.

Cash outflow elements

The four outflow elements driving change in IRR comprise:

- R&D cost – changes to R&D costs for self-originated assets
- 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 assets under review
- tax rates – alterations to the company specific tax rates based on average effective tax rates over the historical ten-year period.

The annual impact of each factor for the cash outflows has been run through into the models in isolation so that their individual impact on the IRR can be quantified.

Cash inflow elements

The inflow elements driving change in IRR comprise:

- forecast revenues, which, in the case of dynamic returns can be further split into:
 - terminated – loss of forecast revenues from late-stage pipeline due to termination of assets
 - approved – transfer of forecast revenues to the commercial portfolio as assets launch and therefore leave the late-stage pipeline
 - existing – increases or decreases in forecast revenues for assets which remain within the late-stage pipeline
 - new – forecast revenues associated with new assets entering the late-stage pipeline.
- margin – changes in a company's average cash operating margin.

The annual impact of each factor on the cash inflow has been analysed in isolation so that their individual impact on returns can be quantified.

Model inputs: R&D cash outflows

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

Self-originated assets

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; Deloitte and GlobalData proprietary data was used for 2016 (see Figure 2). This methodology incorporates the cost of failure or asset attrition from the 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 the most recent year end for each of the companies in question.

Figure 2. Industry average benchmarks 2016

Industry average benchmarks	R&D cost allocation	R&D cycle times
Discovery to first toxicity dose	24%	35%
Preclinical to Phase II	28%	40%
Phase III and submission	48%	25%

Source: Deloitte and Global Data proprietary data

Assets acquired through in-licencing

For assets which have been in-licensed from a third party, any upfront payments have been included in the relevant year of acquisition. In-licencing 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 assets have been assumed to be incurred at their maximum potential amounts on commencement of sales of the assets. Any costs expended in developing the product subsequent to the in-licencing have been included as per the internally developed assets.

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

For deals involving a basket of assets, deal values have been weighted according to the number of assets 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.

Assets acquired as part of a business combination

The method applied to account for R&D costs incurred as part of a business combination varies based on materiality of the transaction 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 assets noted above
2. Where the acquired company has: reasonably stable historic R&D spend; reasonably stable historic operating margins (i.e. has a significant commercial portfolio); and is considered of a material size, a full consolidation approach is taken. This means R&D costs prior to the date of the business combination have been included separately in the model based on publicly available annual reports and applicable GAAP at the time results were issued (either local GAAP applicable in the country of incorporation, IFRS or US GAAP)
3. Where acquired companies did not meet the definition above acquired in-process R&D figures were taken as the figure paid for the R&D portfolio. This separates the value of the R&D pipeline from any commercial portfolio acquired or net value of the company's assets less liabilities.

The costs associated with assets acquired as part of a business combination have not been included independently as these are captured via the inclusion of the acquired company's pre-acquisition R&D cost or IPR&D. Further, publicly available data does not typically include the fair value attributed to each of the assets acquired. Any costs expended in developing the product subsequent to the business combination have been included as per the internally developed assets.

Model inputs: forecast cash inflows

Sales forecasts

1. Asset sales were forecast for a 21-year timeframe for each time period under investigation
2. 2016 revenue forecasts were calculated by GlobalData using a combination of forecasting methodologies, including analyst consensus forecasts and proprietary patient-based forecasting models
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 of the report year; forecasted revenues are based on knowledge and events as of this date
5. After reaching peak sales, standard erosion curves were applied depending on the type of asset considered. Different erosion curves have been developed for each asset 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 asset. Accurate patent data can be difficult to locate, therefore a number of rules were defined to ensure consistency across the assets.

Margin applied to sales forecasts

Inflows have been determined by applying an average un-leveraged cash flow adjusted operating margin. This has been calculated using operating profits reported in publicly available company reports over the three years preceding each year.

Modelling assumptions

The use of forecast data and publicly available information regarding pipelines and deal information presents certain challenges and risks. These challenges and risks include, but are not limited to, the following:

1. The late-stage pipeline is an accurate reflection of the pipeline, as of 30th April in the year of the report. This incorporates all public information available at that date. There is often a lag in obtaining intelligence on product launches, particularly of line extension products, and intelligence on new Phase III compounds entering the late-stage pipeline. This may mean products are removed from the pipeline the year following launch or may have a delay in pipeline inclusion until the year following Phase III entry
2. Deal and licensing information is commercially sensitive and therefore exact financial information is limited. During the research phase several proprietary databases combined with publicly available information have been used to construct a picture of the costs associated with compounds. It is important to note however that not all in-licensing and deal financial information is available outside of the companies involved, therefore some deal information used within this study does not have financial values associated with it
3. All forward-looking statements reflect knowledge and information available as of 30th April and are not updated post publication
4. The revenue and portfolio information provided in this paper constitute forward-looking statements relating to the financial, operational and performance of specific companies. Although the authors of this paper believe these forward looking statement are based on reasonable assumptions listed here, any forward-looking statements by their very nature, involve risks and uncertainties. These forward-looking statements may be influenced by factors which affect actual outcomes or results to be materially different from those predicted here
5. In-licensing costs included in the model are limited to those products included in the late-stage pipeline, thus in-licensing costs associated with compounds that failed prior to Phase III are not included
6. 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 each 10 year period. This prevents an assessment of differences in development performance between each organisation, for example, therapeutic area and development programme specific cycle times are ignored and companies with better than average cycle times are not rewarded in this model
7. Historic R&D costs have not been included within the model beyond the most recent year-end for each company
8. The assumption that average cash operating profits over the three year historical time period reflect future margins over the 21 year revenue forecast period may fail to fully reflect the impact of recent corporate cost reduction initiatives where relevant
9. Revenue forecasts have been risk-adjusted using historical Phase III and submission success rates that may not model potential future changes in the regulatory and payer environment
10. The model is sensitive to the distribution of compounds across the late-stage pipeline (Phase III to submission) and as this drives cash flow timing, a snapshot taken in a different year could generate different results.
11. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of patents, marketing exclusivity or trademarks; the risk of substantial adverse litigation/ government investigation claims and insufficient insurance coverage; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any failure by third parties to supply materials or services; the risk of failure to manage a crisis; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; the risk of environmental liabilities; the risks associated with conducting business in emerging markets; the risk of reputational damage; and the risk of product counterfeiting. Nothing in the report or analysis should be construed as a profit forecast.

Notes



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