REFERENCE CODE **GDHC006PLR** | PUBLICATION DATE **MARCH 2015**

GlobalData
PharmaLeaders

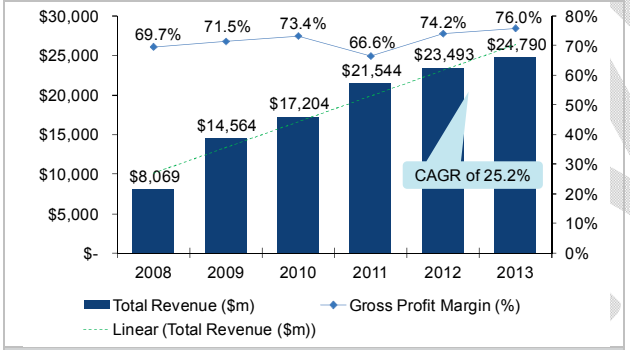
MID-CAP BIOTECHNOLOGY BENCHMARK REPORT – SALES FORECASTS AND PRODUCT VALUATIONS OF INNOVATIVE BIOTECHS

Executive Summary

Robust Fundamentals Instill Investor Confidence in the Biotech Sector

According to GlobalData's *Mid-Cap Biotechnology Benchmark Report,* the combined total revenue and average gross profit margin for the peer group of 35 biotech companies increased from 2013 to 2012. As illustrated below, revenue for this peer group came in 5% higher in 2013, at $24.8 billion, than in 2012. From 2008–2013, the total revenues for this peer group increased at a Compound Annual Growth Rate (CAGR) of 25.2%, which drove the average gross profit margin up by 180 basis points to 76%.

Mid-Cap Biotech Peer Group, Total Revenue ($m) and Average Gross Profit Margin, 2008–2013



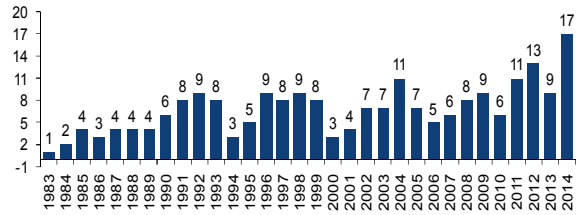
Source: GlobalData, Pharma eTrack [Accessed October 7, 2014] and company SEC filings

The increase in the biotech peer group total revenue in 2013 was driven by Regeneron and Actelion, both of which posted nearly $2 billion in sales in 2013. Regeneron's sales grew by 53%, as the company continued its commercialization of Eylea (afilibercept) in markets outside the US, including for the drug's third and most recently approved indication for the treatment macular edema secondary to central retinal vein occlusion (CRVO), in both the EU and in Japan. Actelion also contributed to the increase in the total peer group revenue, with better-than-expected sales of Tracleer (bosentan), the company's endothelin receptor antagonist (ERA) for treating pulmonary arterial hypertension (PAH). Actelion's $250m purchase of Ceptaris and its lead asset, Valchlor (chlormethine), also drove this increase. Meanwhile, Pharmacyclics was the peer group revenue growth leader in 2013, with sales increasing by $260m (217%) as a result of additional licensing revenues generated by the approval of Imbruvica (ibrutinib).

Historic Number of Orphan Drugs Approved in 2014

In 2014, the FDA's Center for Drug Evaluation and Research (CDER) approved 17 New Molecular Entities (NMEs) for orphan drugs, the highest number since the Orphan Drug Act was passed in 1983.

Number of Orphan Drugs Approved, 1983–2014



Source: FDA Center for Drug Evaluation and Research, New Drug Review, 2014 Update [Accessed December 11, 2014]

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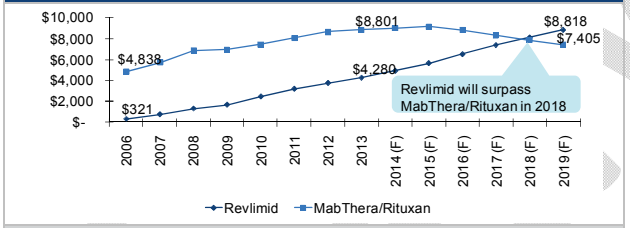
Celgene's Revlimid Will Eclipse Roche's MabThera/Rituxan by 2018

While Roche's MabThera/Rituxan (rituximab) was the top-selling orphan drug in 2013, its US patent was issued in 1998 and is expected to expire in 2015. However, as with many biologics, GlobalData does not anticipate a large drop-off in sales of Rituxan, and Roche's market share and commercialization heft will help protect these sales from the effects of competitor entry. However, that being said, we do expect Rituxan's overall dominance of the orphan drug market to wane slightly beginning in 2015, and give way to Celgene's Revlimid (lenalidomide) as the top-selling orphan drug by 2018, with the latter posting over $8.8 billion in sales by 2019.

Revlimid vs. MabThera/Rituxan Sales ($m), 2006–2019



Source: GlobalData, Pharma eTrack [Accessed August 11, 2014] and analyst consensus estimates

Celgene had a busy year in 2013, seeking additional indications for Revlimid, its flagship product. Celgene's international operations announced in 2013 that Revlimid had received approval from the China State Food and Drug Administration (SFDA) for use in combination with dexamethasone as a treatment for patients with relapsed or refractory multiple myeloma who have received at least one prior therapy. Later in the year, in April, the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for Revlimid for the treatment of patients with transfusion-dependent anemia due to low-to-intermediate risk myelodysplastic syndromes (MDS) when other therapeutic options are insufficient. Lastly, in June 2013, the FDA approved the drug for mantle cell lymphoma (MCL), a rare and aggressive type of blood cancer.

Regeneron's Sales Expected to Top $6 Billion by 2019

Since Eylea's initial US approval for the treatment of neovascular (wet) age-related macular edema (AMD) in November 2011, Regeneron has been partnering with large pharma companies, such as Roche, Bayer, and Sanofi, to successfully expand the drug's treatment label to include additional diseases of the eye, such as diabetic macular edema (DME) and macular edema following retinal vein occlusion (RVO), which includes branch retinal vein occlusion (BRVO). Eylea has received approvals in Colombia, Australia, the EU, and Canada. The company also made agreements with Santen Pharmaceuticals and Bayer Yakuhin to drive the commercialization of Eylea in Japan, and on November 18, 2014, Bayer received approval for Eylea for DME in that country. Due to the drug's commercial success, GlobalData expects Eylea

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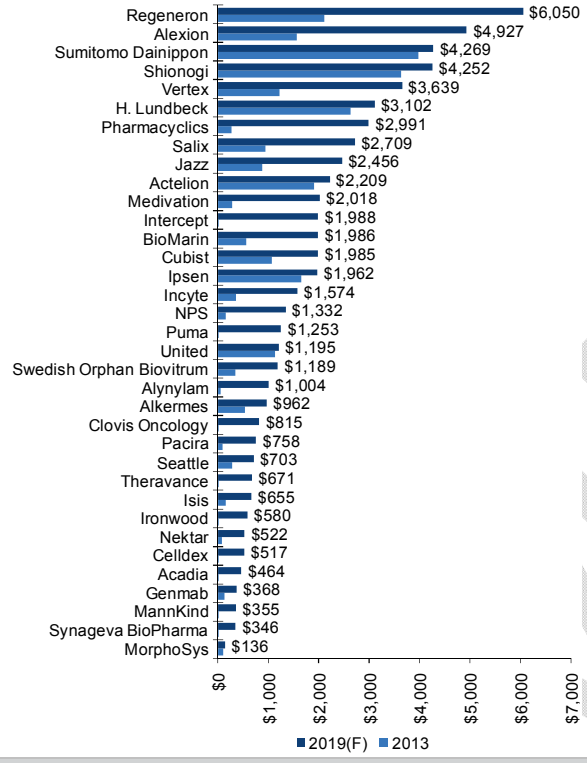
sales to fuel Regeneron's top-line growth to over $6 billion by 2019.

Mid-Cap Biotech Peer Group, Company Sales ($m), 2013 vs. 2019

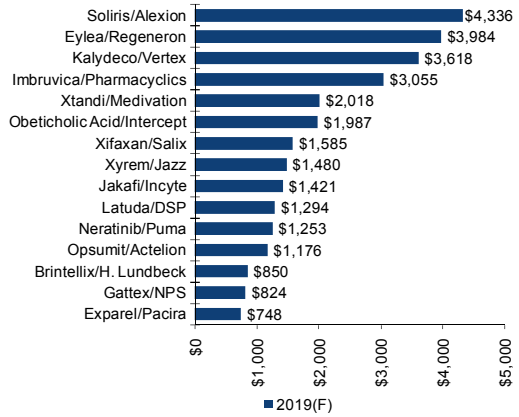


Source: GlobalData Pharma eTrack [Accessed October 7, 2014] and company SEC filings
F = forecast

Alexion's Soliris Will Be the Top Seller in the Biotech Peer Group by 2019

On March 16, 2007, the FDA approved Alexion's Soliris (eculizumab) for the treatment of all patients (adults and children) with paroxysmal nocturnal hemoglobinuria (PNH). A few months later, on June 22, the EMA granted marketing approval for Soliris in Europe for the same indication and patient population. In January 2009, Soliris received an orphan drug designation for the treatment of PNH in Japan, and the following August, the FDA and EMA granted Soliris an orphan drug designation for the treatment of atypical hemolytic uremic syndrome (aHUS). Since then, Alexion has been expanding the drug's territory coverage to include Canada, and Australia submitting applications to include children suffering from PNH and aHUS.

Mid-Cap Biotech Peer Group, Product Forecasts ($m), 2019



Source: GlobalData Pharma eTrack [Accessed October 7, 2014] and company SEC filings
F = forecast

Increasingly Competitive Environment Drives Deal Values and Price Premiums

The total deal values in the biotech sector soared to over $82 billion in 2013, an increase of 168% compared with $30.6 billion in 2012. The rise in the total deal values in 2013 was the result of significant consolidation in the biotech sector, as the space experienced a number of mid-sized

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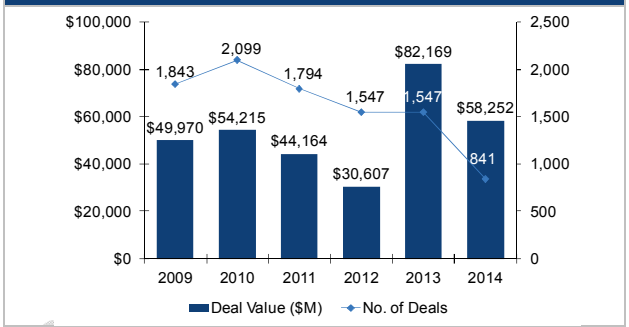
mergers and acquisitions (M&As), particularly in the oncology, immunology, and infectious diseases therapeutic categories. Of the upfront payments disbursed in 2013, Cubist and Auxilium paid out the most in total upfront payments as a result of acquisitions. Cubist paid $1.3 billion in total upfront payments, including $704m to acquire Trius Therapeutics and its late-stage antibiotic, tedizolid phosphate (TR-701), which is being evaluated as a potential treatment for certain Gram-positive infections, including methicillin-resistant *Staphylococcus aureus* (MRSA). Cubist also paid $551m to buy Optimer Pharma and its lead asset, Dificid (fidaxomicin), an antibacterial drug to treat *Clostridium difficile*-associated diarrhea (CDAD) in adults 18 years of age or older. Meanwhile, Auxilium paid $585m upfront to buy Actient Pharmaceuticals, a urology therapeutics company, from the private equity firm, GTCR Golder Rauner, LLC. This transaction augmented Auxilium's male health portfolio, adding Testopel (testosterone pellets), an implantable testosterone replacement therapy, and Edex (alprostadil), an injectable drug for erectile dysfunction. It's also noteworthy that, in October 2014, Endo purchased Auxilium for $2.6 billion, representing a price premium of 55% above Auxilium's closing stock price, and Cubist was acquired by Merck the following December for $9.5 billion, representing a 35% premium over Cubist's five-day average trailing share price.

Biotechnology Sector, Total Number of Deals and Deal Values ($m), 2009–2014



Source: GlobalData Pharma eTrack, [Accessed October 7, 2014] and company data

Note: Includes all M&As, asset transactions, and licensing deals. Deal values are included wherever disclosed.

In addition to Cubist and Auxilium, a couple of other biotechnology companies contributed to the total upfront payments disbursed in 2013. Clovis Oncology paid $200m upfront ($420m in total) to purchase Italy-based EOS, a biotechnology company focused on cancer therapeutics, and its development pipeline, which includes programs for treating ovarian, colon, and renal cancers. EOS' lead asset, lucitanib (E-3810), was in Phase II for the treatment of solid tumors, including breast cancer and squamous non-small cell lung cancer (NSCLC). Also, Isis paid Biogen Idec $100m upfront as part of a six-year research and development (R&D) agreement to develop antisense drugs to treat neurological disorders.

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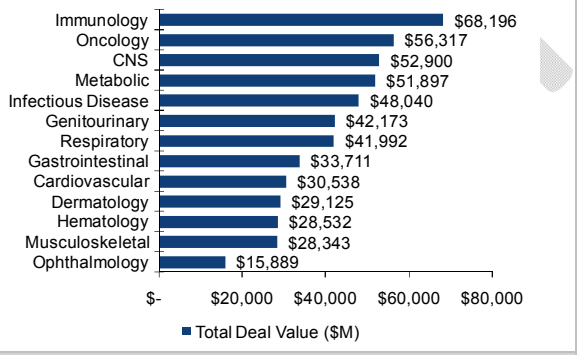
Immunology and Oncology Remain "Hot" Markets for Financial Investment

Not surprisingly, the oncology and immunology franchises witness the most deals activity, as these are fast-growing therapeutic areas with high unmet needs that draw considerable financial investment across the industry. As illustrated below, the top three franchises from 2010 through 2014 were immunology ($68.1b), oncology ($56.3b), and CNS ($52.9b). These high deal values were the result of a number of large M&As; Amgen's $10.4 billion acquisition of Onyx, and Shire's $2.7 billion transaction for ViroPharma, contributed to the deal valuations in 2013. On the licensing front, Celgene is continuing its partnering spree to develop and commercialize products for treating multiple myeloma and inflammatory diseases, such as Crohn's disease.

Biotechnology Sector, Total Deal Value ($m) by Therapy Area, 2010–2014



Source: GlobalData Pharma eTrack [Accessed October 7, 2014] and company SEC filings

Note: Includes all M&As, asset transactions, and licensing deals. Deal values are included wherever disclosed.

A number of large CNS deals were signed in 2014, including Acorda's purchase of Civitas Therapeutics for $525m, giving the former a Phase III drug for Parkinson's disease complications. Jazz Pharmaceuticals continued on its strategic focus in the CNS category, complementing its marketed product, Xyrem (sodium oxybate), by acquiring Aerial Biopharma for $125m. Both Xyrem and ADX-N05 are for the treatment of excessive daytime sleepiness in patients with narcolepsy. Meanwhile, Roche's $8.3 billion acquisition of InterMune is the company's largest since it acquired Genentech back in 2009. Also, the fold-in of Idenix Pharma gives Merck a cadre of anti-hepatitis C virus (HCV) drugs, which the company hopes will gain share in an increasingly crowded HCV market after Gilead's blockbuster launch of Sovaldi (sofosbuvir) in December 2013.

Top Asset Valuations: Eylea, Soliris, and Kalydeco Secure Long-Term Cash Flow

The figure below displays the Net Present Value (NPV) of the leading products across the mid-cap biotech peer group. Regeneron's Eylea, Alexion's Soliris, and Vertex's Kalydeco (ivacaftor) had the largest NPV, based on each company's market cap, stock price, discount and tax rates, and cost parameters. This also means these products will drive significant cash flows for these companies over the lifetime of the assets.

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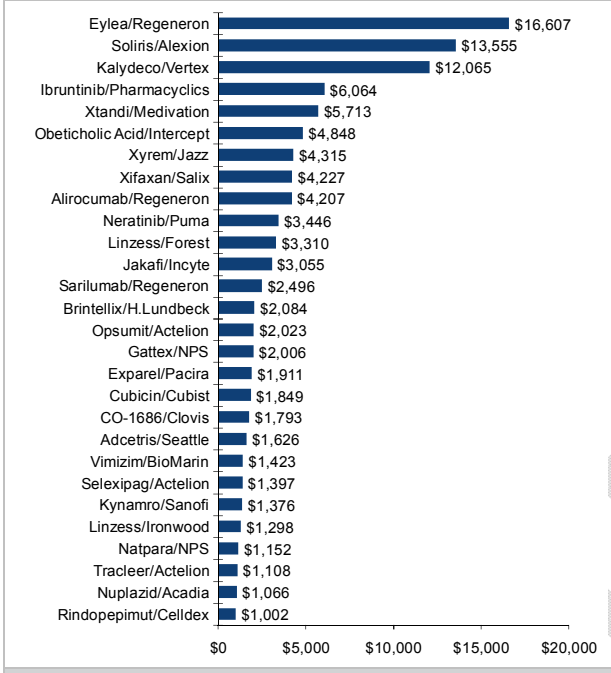
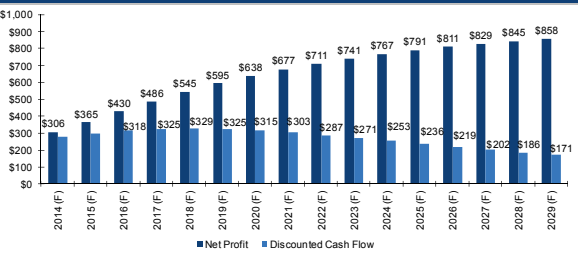
Mid-Cap Biotech Peer Group, Leading Products, NPV ($m),



Source: GlobalData, Pharma eTrack [Accessed October 7, 2014] and company SEC filings

Jazz Pharmaceuticals, Xyrem, Net Profit and DCF ($m), 2014–2029



Source: GlobalData, Pharma eTrack, [Accessed October 7, 2014] and company SEC filings

F = forecast

The figure below illustrates the net profit forecast, and discounted cash flow (DCF) for Jazz Pharmaceuticals' top asset, Xyrem, over the 15-year period from 2014 through 2029.

Clinical Pipelines: BioMarin, Actelion, and Incyte

BioMarin is currently conducting over 100 clinical trials across its pipeline. Of the 123 clinical trials, 45 (37%) are in late-stage (Phase III or later) development, 38 of which are being evaluated for metabolic disorders. BioMarin has 16 clinical trials for Phenylketonuria (PKU) and 17 clinical trials for Mucopolysaccharidosis (MPS) disorders. The figure below displays the number of clinical trials being conducted by BioMarin by phase, as of October 7, 2014.

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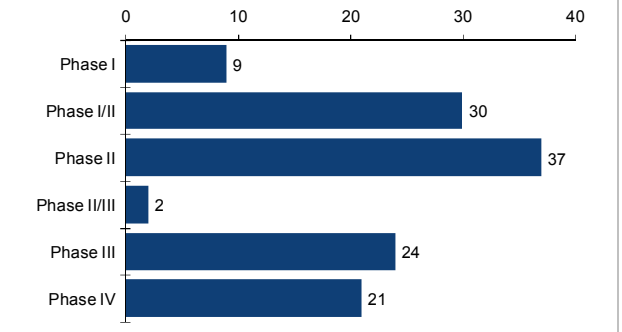
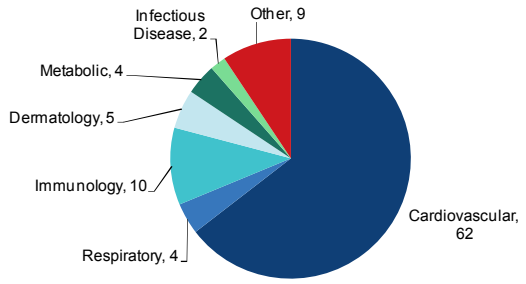
BioMarin, Number of Clinical Trials by Phase



Source: GlobalData, Pharma eTrack [Accessed October 7, 2014] and company SEC filings

Actelion, Number of Clinical Trials by Therapy Area

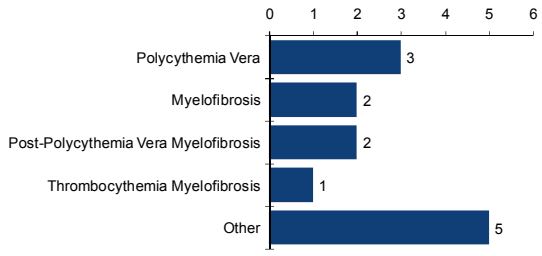


Source: GlobalData, Pharma eTrack [Accessed October 7, 2014] and company SEC filings

Actelion currently has 29 pipeline products accounting for 226 clinical trials either completed or ongoing. Tracleer (bosentan) is the company's lead pipeline asset being evaluated in 65 clinical trials, mostly for cardiovascular indications. Actelion has 44 clinical trials for treating pulmonary arterial hypertension, and four clinical trials for Eisenmenger Syndrome, a condition that affects blood flow from the heart to the lungs caused by a congenital heart defect where people are born with a hole between the left and right ventricles of the heart. The figure below displays the number of clinical trials being conducted by Actelion by therapy area, as of October 7, 2014.

Incyte's lead asset, Jakafi (ruxolitinib), is under development mostly for oncological and hematological disorders such as Polycythemia Vera and Myelofibrosis. The figure below displays the number of clinical trials being conducted by Incyte in the hematology indication as of October 7, 2014.

Incyte, Number of Clinical Trials by Indication, Hematology



Source: GlobalData, Pharma eTrack [Accessed October 7, 2014] and company SEC filings

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2 Introduction

2.1 Report Scope

GlobalData's *Mid-Cap Biotechnology Benchmark Report* applies our proprietary ranking methodology to compare the competitive positions of 35 mid-cap biotechnology companies on 14 financial metrics. These companies are analyzed based on their financial performance, research and development (R&D) spending, capital structure, and firm utilization to illustrate the different strategies they are using to increase value for their shareholders and create a competitive advantage. Throughout the report, GlobalData's Industry Dynamics Team provides expert insight, expanding on each of the metrics discussed.

In addition to the financial metrics, this report provides an overview of the biotech sector growth rates, and discusses the regulatory approvals that occurred in 2014, along with our forecast sales outlook for each drug. We also examine how the patent cliff will impact the industry moving forward, along with deals and licensing activity, and the prospects for niche/orphan drugs. Lastly, we use our proprietary database tools to determine the Net Present Value (NPV) of both marketed and clinical pipeline assets and their future profits and cash flows.

GlobalData identified these 35 innovative biotech companies to apply its benchmarking methodology, providing a foundation for strategic discussion and analysis. GlobalData's coverage examines these companies from a unique company-centric lens, combining financial performance and resources allocation with partnering activity to assess each company's overall strategy. This type of coverage is unlike any other analysis available, and delivers a consistent view into the evolution of these companies' corporate growth.

Key Questions Answered

- What specific strategies are these innovative biotech companies employing to gain market share?
- What therapeutic areas are these biotech companies focusing their R&D spending on?
- Which trends will affect the biotech sector moving forward?
- How does my pipeline and commercialization strategy match up against the competition?

Introduction

- What specific business development activities are taking place in terms of partnerships or mergers and acquisitions (M&As)?
- What particular enabling technologies and drug platforms are these biotech companies developing?
- How are these biotech companies maximizing their capital spending to gain a competitive advantage?

Key Benefits

This report will enable you to:

- Analyze and track the strategies that biotech companies are using to gain share in the increasingly competitive market
- Understand the underlying financial metrics that differentiate certain companies from the pack in terms of growth and profitability, and spending and asset structure
- Organize your sales and marketing strategy to identify companies with proprietary technologies in order to maximize opportunities for licensing, partnership, investment, or takeover.
- Use this information as an independent source for your due diligence and transaction strategy
- Benchmark your company's performance against a group of similar biotech companies to assess areas of strength and uncover opportunities

2.2 Companies Covered

The 35 companies covered in this report are: Acadia, Actelion, Alexion, Alkermes, Alnylam, BioMarin, Celldex, Clovis Oncology, Cubist, Genmab, H. Lundbeck, Incyte, Intercept, Ipsen, Ironwood, Isis, Jazz, MannKind, Medivation, MorphoSys, Nektar, NPS, Pacira, Pharmacyclics, Puma Biotechnology, Regeneron, Salix, Seattle Genetics, Shionogi, Sumitomo Dainippon, Swedish Orphan Biovitrum, Synageva BioPharma, Theravance, United Therapeutics, and Vertex Pharmaceuticals.

Introduction

2.3 Upcoming Reports

The publication dates for the following reports are to be determined, and the titles are subject to change.

- GlobalData (2015). PharmaSphere: Emerging Biotechnologies: RNAi Therapeutics Market Analysis
- GlobalData (2015). PharmaSphere: Emerging Biotechnologies: Gene Therapy Market Analysis

2.4 Recently Published Reports

- GlobalData (2014). PharmaLeaders: Global Pharmaceutical Market Benchmark Report – Retrospective and Forward-Looking Analysis of Leading Pharmaceutical Companies, October 2014.
- GlobalData (2014). PharmaSphere: North America Market Access Report, December 2014
- GlobalData (2014). PharmaSphere: Emerging Biotechnologies: Stem Cells Market Analysis, November 2014,
- GlobalData (2014). PharmaSphere: Regulatory Frameworks and Product Pipelines in the Global Biosimilars Market, May 2014,
- GlobalData (2014). PharmaSphere: Emerging Biotech Investment Report – Strategic Trends in Private Equity and Venture Capital Funding, March 2014,
- GlobalData (2013). PharmaLeaders: CRO Benchmark Report – Financial Performance Benchmarking and Competitive Landscape Assessment of Leading CROs, August 2013,
- GlobalData (2013). PharmaSphere: Early-Stage Technology Transfer Collaborations – Enabling Platform Technologies & Deal Synergies between Academia and the Pharmaceutical Industry, April 2013,

8 Appendix

8.1 Research Methodology

GlobalData's dedicated research and analysis teams consist of experienced professionals with marketing, market research, and consulting backgrounds in the pharmaceutical industry, and advanced statistical expertise.

GlobalData adheres to the codes and practices of the European Pharmaceutical Market Research Association (EphMRA, ephra.org).

All GlobalData databases are continuously updated and revised. The following research methodology is followed for all databases and reports.

8.1.1 Coverage

The objective of updating GlobalData's coverage is to ensure that it represents the most up-to-date vision of the industry possible. Changes to the industry taxonomy are built on the basis of extensive research of company, association, and competitor sources. GlobalData aims to cover all major news events and deals in the pharmaceutical industry, updated on a daily basis. Company coverage is based on three key factors: revenues, products, and media attention/market potential.

- The estimated revenues of all major companies, including private and governmental, are gathered and used to prioritize coverage.
- Companies that are making the news, or that are of particular interest due to their innovative approach, are prioritized.

8.1.2 Secondary Research

The research process begins with exhaustive secondary research on internal and external sources being carried out to source qualitative and quantitative information relating to each market. The secondary research sources that are typically referred to include, but are not limited to:

- Company websites, annual reports, financial reports, broker reports, investor presentations, and US Securities and Exchange Commission (SEC) filings
- Industry trade journals, scientific journals, and other technical literature
- Internal and external proprietary databases; relevant patent and regulatory databases

Appendix

- National government documents, statistical databases, and market reports; procedure registries
- News articles, press releases, and webcasts specific to the companies operating in the market

Appendix

8.7 Disclosure Information

GlobalData is a product of GlobalData Ltd, a UK-registered company. GlobalData Ltd has no current or intended investment banking or corporate finance relationships or operations. The material presented in this report is provided for information purposes only, and is not to be used or considered as a recommendation to buy, hold, or sell any securities or other financial instruments. No GlobalData Ltd directors, officers, or employees are on the Board of Directors of a covered company, and no one at a covered company is on the Board of Directors of GlobalData Ltd.

8.8 Disclaimer