

In the pipeline

Pharma companies are engaged in pipeline portfolio diversification, with a focus on speciality products for diseases with high unmet needs, including cancers, infectious diseases and immunological disorders. According to **GlobalData's** analysts, 2011 will be another successful year for biological approvals.

The pharmaceuticals pipeline is burgeoning with oncology projects, followed by those in neuroscience, cardio-metabolic and infectious disease sectors. Immunology, inflammatory and respiratory projects are also notable in the pipelines of the top pharmaceutical companies, according to GlobalData's '2011 Pharmaceutical R&D Landscape' report.

Oncology

The oncology pipeline is populated with oral multi-kinase and vascular endothelial growth factor (VEGF) inhibitors and monoclonal antibodies. New oral and injectable products will be of prime importance in the coming years. Multi-kinase and VEGF inhibitors in clinical development include GlaxoSmithKline (GSK)'s Tyverb (Tykerb) and Pfizer's Axitinib, Neratinib and Bosutinib.

Cancer monoclonal antibodies comprise Pfizer's Inotuzumab ozogamicin and Lilly's Ramucirumab. An emerging field in cancer therapy is cancer vaccine development. Cancer vaccines to look out for include Merck's cervical cancer vaccine, BioVex's OncoVEX and Oncocyte's Stimuvax.

Central nervous system

Alzheimer's disease drugs in the pipeline include Janssen's Bapineuzumab, Pfizer's Dimebon and Eli Lilly's LY2062430 (solanezumab). Anti-psychotics for bipolar mania and schizophrenia include Forest's and Gedeon Richter's Cariprazine and GSK's Histamine H3 antagonist.

The anti-depressive pipeline candidates include AstraZeneca's and Targacept's TC-5214, and GSK's Orvepitant. The highlights in the multiple sclerosis pipeline this year include Biogen's BG-12 and sanofi-aventis's Teriflunomide. Analgesics in development include J&J's Nucynta (extended-release formulation), Cerimon's Diclofenac patch, Elite Pharmaceuticals' ELI-154, Transdel Pharmaceuticals' Ketotransdel, Omeros Corp's OMS103HP, Durect's Posidur, Zogenix's ZX002, Pfizer's Lyrica and GlaxoSmithKline's Losmapimod.

Infectious diseases

Vaccine development continues to boom in the infectious disease segment. Hepatitis C drugs in the pipeline include protease inhibitors such as Merck's Boceprevir, and interferons such as

Bristol-Myers Squibb's polyethylene glycol-interferon lambda and Biolex's Locteron. Anti-HIV medications include HIV integrase inhibitors, chemokine receptor antagonists and non-nucleotide reverse transcriptase inhibitors.

Cardiovascular and metabolic

Major cardiovascular therapeutics such as cholesterol-lowering agents and anti-hypertensives face stiff generic competition and will lose considerable market share. The cardiovascular market for 2011 is dominated by anti-thrombotic and anti-platelet products, including Pfizer's Apixaban, Novartis's Elinogrel, Daiichi's Edoxaban and Merck's Vorapaxar and Betrixaban.

The diabetes market is predicted to feature glucagon-like peptide-1 compounds and sodium glucose co-transporter-2 inhibitors. Novel candidates with unique modes of action also feature in the current pipelines.

Eli Lilly's Empagliflozin, sanofi-aventis's Lixisenatide, GSK's Albiglutide and Bristol-Myers Squibb and AstraZeneca's Dapagliflozin are at the forefront of anti-diabetic therapy this year. GSK's Otelixizumab is a type 1 diabetes monoclonal antibody in development. Regulatory guidelines requiring higher patient enrolment in diabetes trials could cause delays in the approval of diabetic drugs already in the pipeline.

Respiratory

The respiratory drug pipeline is dominated by anti-asthmatics and treatments for COPD. Forest Labs' Acclidinium, GSK's Relovair and Novartis's Indacaterol, as well as cystic fibrosis candidates Pharmaxis' Bronchitol and Vertex's VX-770, are some of the drugs for which activity can be expected.

Big Pharma pipelines

GSK has a dense pipeline, with drugs catering to a wide number of diseases. It has many late-stage drugs with several in phases I and II. Infectious diseases, oncology and neurology are the main areas of focus, followed by respiratory and metabolic disorders. The GSK pipeline features many speciality drugs, the majority of



which are monoclonal antibodies and vaccines for cancers and infectious diseases. Vaccine development for infectious diseases also features. GSK's anti-malarial, tafenoquine and influenza candidate Relenza is in the company's extensive anti-infective pipeline, along with many infectious disease vaccines. The anti-inflammatory/respiratory pipeline covers COPD, asthma and Crohn's disease. Type 2 diabetes and age-related macular degeneration (AMD) appear to be the focus in the metabolic and ophthalmology segments, respectively.

One of the vast drug pipelines is that of **Pfizer**, which features over 100 candidates with more than 20 in phase III and a significant number in registration. Pfizer's acquisition of Wyeth has broadened the former's portfolio, with oncology, neurosciences and cardiovascular drugs populating the pipeline, and significant numbers of candidates under development for respiratory/allergy and inflammatory disorders. Pfizer's speciality drug focus covers many biologics, including vaccines catering for areas such as cancer, Alzheimer's disease, ophthalmology,

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inflammation and infectious diseases. Ophthalmology drugs are targeted at AMD, diabetic macular degeneration and edema. Pfizer's allergy and respiratory pipeline features drugs for asthma and COPD, with type 2 diabetes reigning in the metabolic sector. Anti-inflammatories are centred on rheumatoid arthritis, psoriasis and inflammatory bowel disease, while anti-infectives include antibacterials for *Staphylococcus aureus* infections, pneumococcal disease and tuberculosis, antivirals for hepatitis C virus infections, and antiparasitics for malaria and onchocerciasis.

Sanofi-aventis's pipeline contains more than 50 projects in clinical development. Phase I and II candidates constitute the majority of the company's pipeline projects, with over 15 in phase III and beyond. The salient feature of the sanofi-aventis pipeline is the focus on infectious diseases, oncology and neurological domains. Biologics are prominent, with anti-cancer monoclonal antibodies and infectious disease vaccines under development. Drugs are being developed for neurological disorders such as multiple sclerosis, depression, Alzheimer's disease and pain. Diphtheria, tetanus, pertussis, dengue, meningococcal and influenza vaccines, anti-diabetics, antineoplastic agents and antithrombotics are some of the advanced therapeutics under development.

With its acquisition of MedImmune and Novexel, **AstraZeneca** has a robust pipeline focused on producing small molecules, vaccines and biologics to address unmet medical needs in oncology, neuroscience, respiratory and inflammation, infection, cardiovascular and gastrointestinal areas. Asthma, COPD and rheumatoid arthritis are some areas of interest in the respiratory and inflammation sector. Anti-infectives include vaccines and

Table 1. Biologics that cleared FDA approval this year.

Biologic	Company	Condition
Benlysta	Human Genome Sciences and GlaxoSmithKline	Systemic lupus erythematosus
Yervoy	Bristol-Myers Squibb	Metastatic melanoma
Corifact	CSL Behring	Congenital factor XIII deficiency
Anascorp	Rare Diseases Therapeutics	Treatment of scorpion envenomation
Viibryd	Merck and Forest	Major depressive disorder in adults
Edarbi	Takeda	Hypertension in adults
Daliresp	Forest and Nycomed	COPD exacerbations
Horizant	GSK and XenoPort	Restless leg syndrome
Zytiga	J&J	Late-stage prostate cancer
Promacta (full approval)	GSK	Chronic immune (idiopathic) thrombocytopenic purpura
Tradjenta	Boehringer Ingelheim and Lilly	Type 2 diabetes
Victrelis	Merck	Hepatitis C infection
Edurant	J&J	HIV-1 infection
Incivek	Vertex	Hepatitis C infection
Dificid	Optimer	Clostridium difficile-associated diarrhoea
Potiga	GSK and Valeant	Epilepsy
Nulojix	BMS	Kidney transplant
Arcapta Neohaler	Novartis	COPD
Xarelto	Bayer and J&J	Reduction of risk of blood clots after hip and knee replacements
Brilinta	AstraZeneca	Reduction of cardiovascular death and heart attack in acute coronary syndrome patients

antibodies for viral and bacterial diseases. The oncology pipeline features kinase inhibitors and antibodies. Pain, depressive disorders, Alzheimer's disease and attention-deficit disorder are prominent in neuroscience drug development.

Merck's pipeline showcases more than 30 drugs from phase II to registration stages. The key therapeutic areas of focus are oncology, neurosciences and ophthalmology, infectious diseases, cardiovascular, diabetes and obesity, respiratory, immunology, dermatology, women's health and endocrinology. Merck is developing biological molecules in the areas of cancer, infectious diseases and women's health.

With a pipeline featuring 140 projects and with 16 important filings last year, **Novartis** is actively involved in biologics research, with a significant portion present in exploratory development. Advanced stage candidates include drugs for

depression, myelofibrosis, heart failure, pathologic myopia, infectious diseases and pulmonary arterial hypertension.

Bristol-Myers Squibb (BMS) has a pronounced oncology pipeline, with the majority of cancer drugs present through all the stages. The takeover of Medarex and Kosan Biosciences strengthened BMS's cancer and immunology portfolio. Other major areas of focus are cardiovascular, metabolic disorders, immunology, neurology and infectious diseases, with specific focus on indications including atherosclerosis/thrombosis, Alzheimer's disease, diabetes, obesity, HIV/AIDS and rheumatoid arthritis. The pipeline has become more voluminous since 2009, with around one-third of the compounds in development being biologics. BMS actively seeks to engage in partnerships to mitigate risks and focus on bigger development programmes across various therapeutic areas.

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Eli Lilly is engaged in generating treatments for diseases such as cancer, diabetes, osteoporosis, arthritis and Alzheimer's. Oncology tops the company's clinical pipeline, followed by CNS for depression, Alzheimer's disease, schizophrenia and alcohol dependence. Anti-diabetic and rheumatoid arthritis drugs also feature in Lilly's clinical programmes. Biological drugs occupy a considerable share of the clinical pipeline and dominate the cancer therapeutic segment.

J&J's pharmaceutical segment is focused on drugs for cancer and neurology, including pain management and anti-psychotics, infections, cardiovascular, contraception, dermatology, hematology, gastrointestinal, urology and immunology. Oncology, cardiovascular and CNS therapies are at the forefront of J&J's clinical R&D focus.

Pharma R&D strategies

The pharmaceutical and biotechnology pipelines for 2011 are brimming with projects that strongly feature oncology, neurology and anti-infective products. Complexities in the clinical study design for these drugs, including larger patient enrolment, patient sustenance and protocol complications, result in trial initiation delays and high costs.

Biologics are becoming more prominent across the pipelines of many companies especially in oncology, immunology and infectious diseases. The number of biological approvals is also on the rise, with 2011 bearing bright prospects for biological approvals. Companies are interested in investing in biologics, despite the associated high costs, development times and stringent regulatory measures.

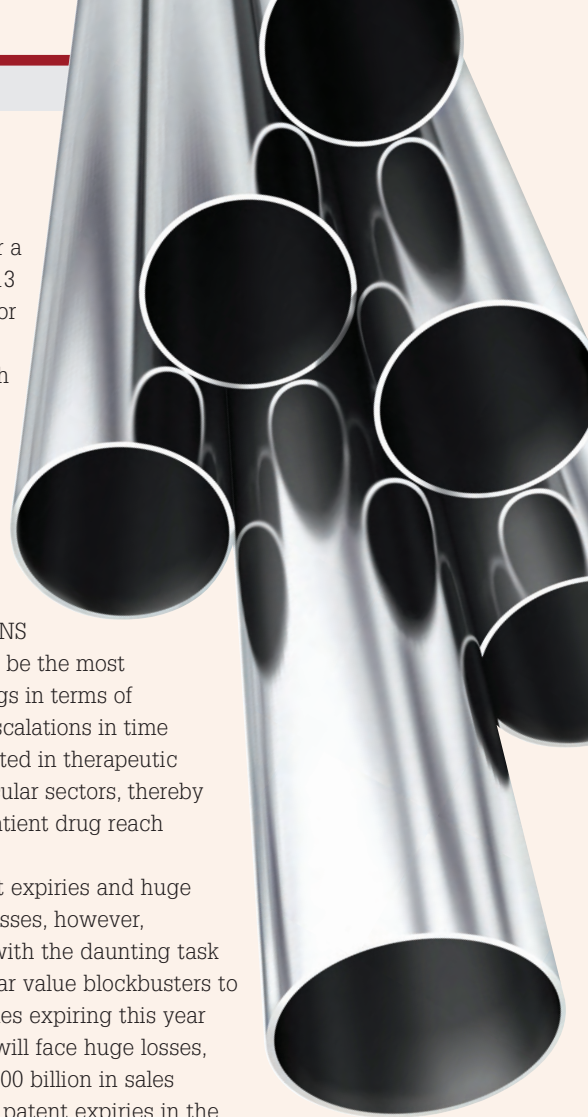
There is tightened control over pharmaceutical R&D spend as drug development costs are spiralling, with related expenses translating into billions of dollars. Growth in R&D investments

has slowed. With the average time to deliver a drug to market being 13 years, the time taken for neurology or oncology drugs, which have high market demands, is around ten years. Antineoplastic agents usually consume the most development time, followed by neurological and anti-infective drugs. CNS drugs are estimated to be the most expensive class of drugs in terms of development. Rapid escalations in time and cost can be expected in therapeutic development for particular sectors, thereby causing setbacks in patient drug reach and patient care.

With looming patent expiries and huge impending financial losses, however, companies are faced with the daunting task of creating billion-dollar value blockbusters to compensate for the ones expiring this year onwards. Companies will face huge losses, with approximately \$100 billion in sales predicted to be lost in patent expiries in the next few years.

The number of pipeline entries is also dwindling and the quantity of new drug applications has decreased over the past two years due to drug failures and subsequent pipeline attritions. Pharmaceutical companies are aggressively devising counter R&D strategies to cope with abundant pressures to eliminate unsuccessful candidates, enhance the speed of drug development and reduce R&D expenditure.

Strategies to recompense the financial setbacks include mergers and acquisitions, in-licensing and collaborations, increased focus on specialty medicines and emerging markets, cost-cutting initiatives across the production chain and the adoption of new drug discovery technologies. Nevertheless, given the stringent regulatory measures, dipping new drug approval rates and incessant surges in drug development time and cost, pharmaceutical companies will have a long way to go to overcome development and regulatory obstacles in order to generate successful returns on investment. ■



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