Bridging the innovation gap...

New Drug Futures:

Products that could change the pharma market to 2013 and beyond

Over 70 pipeline prospects in 8 major therapy areas are analysed in this report

- **Anti-infectives**
- **Cardiovascular**
- **CNS**
- **Gastrointestinal**
- **Metabolic**
- **Musculoskeletal**
- **Oncology**
- **Respiratory**

This new major and insightful 450 page analysis evaluates, compares and contrasts the prospects for the development compounds that could revolutionise the pharmaceutical industry over the next 5 years and beyond.

The report provides:

- Detailed background and market context for each therapy area covered:
  - *Addressable patient population*
  - *Current treatments*
  - *Sales drivers*
  - *Sales breakers*
  - *Future treatments*
  - *Market dynamics – winners and losers*
  - *Key drug launches by 2013*
- Unique sales forecasts by major product to 2013
- Over 70 key products assessed
- Unique evaluation scores for key areas such as novelty of mechanism, clinical data and competition
- Critical and detailed appraisal of each product's research and development
- Extensive pipeline listings, putting the profiled products into their competitive context

The search – and need – for new products has never been greater and what's in the development pipeline has never generated more interest.

That is why this analysis is so important!

THE GLOBAL PHARMA MARKET IN CONTEXT

Are there too many prophets of doom ready to write-off the research-based pharma industry in the future?

Too few novel products and an aggressive generic sector are taking their toll

There is plenty on which to base such anxiety. The research-based industry must achieve a fair price in the face of greater cost control, while the burden of regulation is setting the bar high for successful product introduction. Meanwhile, the generics sector is eating away at ageing and established portfolios.

It is a fair assessment to say that the industry has rested too much on its laurels and successful product portfolios. For too many years, too few novel medicines have been brought to market, laying the foundations for the industry's current ills.

Can it be different?

Biologicals are set to take centre stage

The increasing number of biologicals that are coming to market have real potential for clinical and commercial progress, and while there is an innovation gap until new biological products make their market presence felt, there are considerable reasons to view the future more positively. A considered evaluation of the research pipeline shows that the future can be brighter than many pundits predict.

Winning products

We analyse 8 key therapeutic categories:

Anti-infectives	**Cardiovascular**
CNS	**Gastrointestinal**
Metabolic	**Musculoskeletal**
Oncology	**Respiratory**

Essential analysis of 73 promising products that could change the face of the pharmaceutical industry

Over 70 winning drugs have been identified that could be launched by 2013. Products come from over 35 companies, ranging from multinationals and specialty pharma, to biopharmaceuticals and biotechnology companies.

Will they make it?

Our estimates assume products will gain approval for the indications we have forecast in the timeframe analysed. However, regulatory demands and pressures on cost and development budgets increasingly mean safe and effective medicines are not brought to market. That is why we provide a unique analysis of each product, examining its novelty of mechanism, clinical data, competitive environment, the experience of the developer and risks associated with development within that therapeutic class.

This report is essential reading for industry planners and investors

Anyone wanting an insightful analysis of the products and companies that will shape the global pharmaceutical industry over the next 5 years need look no further than this report.

Anti-infectives

Growth is expected in line with the market average for the anti-infectives therapeutic area, with a forecast 2008-13 CAGR of 3%. Stronger than average growth for anti-HIV agents will be seen with strong uptake of new products such as Gilead Sciences' Atripla, but this is countered by a flat market for antibiotics, and below average growth for other anti-infective agents. We forecast a 1% CAGR for the anti-infectives market for the 2008-2013 period, powered primarily by the market for HIV, for which we forecast a 5% CAGR. There are a number of factors driving growth in the anti-infectives market:

- Growth of resistance in the antibiotics market and introduction of new agents
- Increased incidence of serious fungal infections and development of new agents
- New innovative therapies in the HIV market.

Antibiotics

The most common cause of infections worldwide is respiratory tract infections, which account for 60% of the market. This is followed by urinary tract infections. Also common are skin and skin structure infections, and gastrointestinal/biliary infections.

The worldwide antibiotic market was worth US$26 billion in 2007, of which approximately half the value was accounted for by sales of branded prescription products, and the remainder generic items. Approximately one-third of the market is for hospital-treated infections, while outpatients account for the remainder. The top-selling product worldwide is Johnson & Johnson's Levaquin (ofloxacin), which retains patent protection in the US until December 2010. Many other major products in this category face generic competition, which is steadily eroding market value.

Antivirals

The worldwide antiviral market was worth approximately US$16 billion in 2007, of which US$10 billion is accounted for by treatments for HIV. The herpes market is facing intensifying generic competition, which the report estimates was worth US$2.8 billion in 2007, while new products are expected to boost the growing hepatitis B market (estimated 2007 value US$1 billion) and the hepatitis C market (estimated 2007 value US$2.5 billion).

Antifungals

The antifungals market is another market facing increasing levels of generic competition. We estimate that the prescription antifungals market was worth US$7 billion worldwide in 2007, with possibly another US$3 billion of sales on the OTC market (these are not included within the report). Major new products within this market include Pfizer's Vfend (voriconazole) and Gilead Sciences/Astellas' Mycamine (micafungin).

Major Products Evaluated and Forecast to 2013

- **Albuferon** (albinterferon alpha-2b) *(Novartis/Human Genome Sciences - Hepatitis C)*
- **boceprevir** (SCH 503034) *(Schering-Plough - Hepatitis C)*
- **elvitegravir** (GS 9137) *(Gilead Sciences - HIV)*
- **telaprevir** (VX-950) *(Vertex/Johnson & Johnson - Hepatitis C)*
- **vicriviroc** (SCH-417690) *(Schering-Plough - HIV)*
- **Zeftera** (ceftobiprole) *(Basilea/Johnson & Johnson - Broad spectrum anti-infectives)*

Answering key business questions...

- What patient benefits underpin the expectations for Novartis' hepatitis C treatment Albuferon?
- What products will contribute to Pfizer's antibiotic business growth?
- What boost has been given to the antibiotic research sector from the increasing levels of hospital-acquired infection?
- What is the 5-year growth forecast for HIV?
- Why is Schering-Plough's hepatitis C protease inhibitor boceprevir expected to generate peak sales of US$2.5 billion?
- How might Schering-Plough's CCR_5 antagonist vicriviroc fair against Pfizer's already launched product Selzentry?
- How might physician practise influence sales of Basilea/ Johnson & Johnson's advanced anti-MRSA cephalosporin Zeftera?
- Which of the products listed above have the highest probability of reaching the market?

Cardiovascular

Cardiovascular (CV) disease remains the number one killer in the US and Europe. Sales of CV drugs cover a multitude of therapeutic drug classes and this report focuses on three key therapeutic segments: dyslipidaemia, hypertension and thrombosis (a category in which we include antiplatelet agents, anticoagulants and antithrombotics). Other agents available are for the treatment of arrhythmia (a sector which may be set for some growth) and congestive heart failure, or are used for a variety of different CV conditions.

The forecast for 2008-13 CAGR is -3% for the CV market. This includes a 2008-13 CAGR of -4% and -6% for the two largest sub-therapeutic areas, hypertension and dyslipidaemia respectively. Generic competition is the key reason for this decline, with US patent protection set to expire on Pfizer's Lipitor (atorvastatin) in 2011, and the hypertension market being impacted by the loss of US exclusivity on Novartis' Diovan (valsartan) and AstraZeneca's Atacand (candesartan cilexetil) in 2012.

Arrhythmia

Despite the unmet need in the arrhythmia market, there are relatively few agents under active investigation for this indication (although there are several for use in prevention of stroke associated with atrial fibrillation – which are covered under thrombosis). sanofi-aventis' new class III anti-arrhythmic agent Multaq (dronedarone) is the closest to market and could generate sales of US$860 million by 2013.

Dyslipidaemia

The sheer size of the cholesterol-lowering market has made it an attractive one for drug companies to target, and a number of approaches are under investigation. Following the success of Zetia (ezetimibe)/Vytorin (ezetimibe+ simvastatin) (Merck & Co/Schering-Plough), a number of other cholesterol absorption inhibitors have been studied. These compounds work in combination with statins to give an additional LDL-lowering effect. sanofi-aventis expects to launch its competing agent in 2011. One approach that continues to receive R&D investment is the cholesteryl ester transfer protein inhibitors, even though this class of agents suffered a setback when Pfizer's torceptrapib was discontinued from development.

Thrombosis

The development of new agents for use in the treatment of disorders involving blood-clotting is probably the most dynamic in the CV market at present. The development of several late-stage agents is making this an increasingly interesting and competitive arena as the treatment of thrombosis remains an area of considerable unmet medical need. A number of approaches are under investigation. Schering-Plough is developing an orally-active thrombin receptor antagonist, while other approaches include the potentially important oral direct Factor Xa inhibitors.

Major Products Evaluated and Forecast to 2013

- **apixaban** (BMS-562247) *(BMS/Pfizer – Thrombosis)*
- **AVE-5530** *(sanofi-aventis – Dyslipidaemia)*
- **azilsartan medoxomil** (TAK-491) *(Takeda – Hypertension)*
- **Brilinta** (ticagrelor) *(AstraZeneca – Thrombosis)*
- **Cordaptive/Tredaptive** (laropiprant+niacin) *(Merck & Co – Dyslipidaemia)*
- **Effient** (prasugrel) *(Eli Lilly/Daiichi Sankyo – Thrombosis)*
- **idrabiotaparinux** (SSR 126517) *(sanofi-aventis – Thrombosis)*
- **Multaq** (dronedarone) *(sanofi-aventis – Arrhythmia)*
- **octaparine** (AVE5026) *(sanofi-aventis – Thrombosis)*
- **Pradaxa** (dabigatran) *(Boehringer Ingelheim – Thrombosis)*
- **SCH-530348** *(Schering-Plough – Thrombosis)*
- **Xarelto** (rivaroxaban) *(Bayer/Johnson & Johnson – Thrombosis)*

Answering key business questions...

- There are 13 agents in late-stage research for dyslipidaemia. Which are the most promising and which companies are developing them?
- What clinical trial results may affect the regulatory approval of sanofi-aventis' oral class III anti-arrhythmic agent, Multaq?
- The ultimate worldwide sales for Bayer/Johnson & Johnson's Factor Xa inhibitor thrombosis treatment, Xarelto, could peak at US$10 billion – what competitive hurdles must it overcome to realise such blockbuster revenues?

Central Nervous System

The worldwide CNS market was worth US$88 billion in 2007. The largest segments of the market are schizophrenia, depression & anxiety and epilepsy, though patent expiries are set to diminish their dominance of the CNS market within the coming 5 years.

Alzheimer's disease

On a 2007 market value of US$5.4 billion, the report forecasts a 2008-13 CAGR for the Alzheimer's disease market of -2%. There are several competing trends in this market. We expect an increase in the number of patients suffering from the disease, as the population ages. In addition, drugs are to be used earlier in therapy (although healthcare payers in some markets, such as the UK, are resisting this).

However, these two positive trends are insufficient to outweigh the loss of patent protection on two market leading products: Pfizer/Eisai's Aricept (donepezil) and Forest Labs' Namenda (memantine). The loss of sales may be offset partially by the launch of Wyeth/Elan's novel therapy bapineuzumab, which we believe has the potential to be a top-selling product with peak sales potential in the order of US$5 billion.

ADHD

A 2008-13 CAGR of 1% is forecast for the ADHD market, representing a considerable slowdown in growth rates to those seen in recent years as the market - which has seen huge increases in patient numbers - starts to mature.

The decline in growth is also partly the result of the maturing of products such as Johnson & Johnson's Concerta (methylphenidate) and Eli Lilly's Strattera (atomoxetine), but also the loss of exclusivity on Shire's Adderall XR (mixed amphetamine salts). The launch of new products such as Shire's Vyvanse (lisdexamphetamine dimesylate) goes some way to offsetting this.

Depression & anxiety

The depression market is set to experience a continuation of the long-term decline. We anticipate a 2008-13 CAGR of -7%, primarily as the result of some major patent expiries. Several major products, including Wyeth's Effexor (venlafaxine), Forest Labs' Lexapro (escitaprolam) and Lilly's Cymbalta (duloxetine) are all set to experience generic competition within the forecast timeframe.

Although new antidepressants such as sanofi-aventis' saredutent and Novartis/Serviers' Valdoxan (agomelatine) are in late-stage development, we are cautious on their likelihood of reaching the market in time to have a significant impact on market growth rates. This is due, in part, to the increasingly safety conscious regulatory stance that has delayed launches in this indication.

Major Products Evaluated and Forecast to 2013

- **almorexant** (ACT-078573) *(GlaxoSmithKline/Actelion) - Insomnia)*
- **bapineuzumab** (AAB-001) *(Wyeth/Elan -Alzheimer's disease)*
- **BG12** (Fumarate) *(Biogen Idec - Multiple sclerosis)*
- **Ciltyri** (eplivanserin) *(sanofi-aventis - Insomnia)*
- **Comfyde** (carisbamate) *(Johnson & Johnson - Epilepsy)*
- **dirucotide** (MBP8298) *(Eli Lilly/BioMS Medical - Multiple sclerosis)*
- **fingolimod** (FTY720) *(Novartis - Multiple sclerosis)*
- **lurasidone** (SM13496) *(Dainippon Sumitomo Pharma - Schizophrenia)*
- **Neurelan** (fampridine-SR) *(Acorda Therapeutics - Multiple sclerosis)*
- **Nuvigil** (armodafinil) *(Cephalon - Narcolepsy)*
- **ralfinamide** (NW-1209) *(Newron Pharmaceuticals - Pain)*
- **retigabine** *(GlaxoSmithKline/Valeant Pharmaceuticals - Epilepsy)*
- **Rikelta** (brivaracetam) *(UCB - Epilepsy)*
- **Saphris** (asenapine) *(Schering-Plough - Schizophrenia)*
- **saredutant** (SR 48968) *(sanofi-aventis - Depression)*
- **tapentadol** (R331333) *(Johnson & Johnson - Pain)*
- **telcagepant** (MK-0974) *(Merck & Co - Headache/Migraine)*
- **Valdoxan** (agomelatine) *(Novartis/Servier - Depression)*

Answering key business questions...

- 14 of the 18 products reviewed in the report are forecast for peak sales of >US$1 billion. Why are expectations so high?
- What are the risks and rewards for Wyeth/Elan's novel Alzheimer's treatment bapineuzumab?

Gastrointestinal

The gastrointestinal (GI) market is forecast for a 2008-13 CAGR of -3%, primarily as a result of patent expiries, which are expected to impact the market for gastro-oesophageal reflux disorder (GORD) and other acid-related GI disorders.

The impact of generic competition

Generic competition to a number of major products is anticipated with Takeda's Prevacid (lansoprazole), Johnson & Johnson/Eisai's Aciphex (rabeprazole) and Wyeth/Nycomed's Protonix (pantoprazole) all likely to impact negatively on market growth within the 2008-13 period. The increasing level of generic competition in the US is continuing to erode sales of older products, such as AstraZeneca's Losec/Prilosec (omeprazole) and is also having a negative pricing pressure on branded drugs, such as AstraZeneca's Nexium (esomeprazole). As a result of this competition, we expect a -8% CAGR for the GORD/acid-related GI disorders market for the 2008-13 period. The development of new agents will help mitigate some of this effect, but the effects will be too small within our forecast period to have a significant impact. Looking to the future, one area that has garnered increasing levels of interest is the development of agents to treat the root cause of GORD (low oesophageal sphincter tone), through a variety of mechanisms.

A brighter future?

We expect a brighter future for the IBD and IBS markets, moving forward, albeit from a smaller base. The development of new agents at higher price points within both markets could lead to substantial growth over the 2008-13 period, and we forecast 11% and 22% CAGRs respectively. Among the future winners are Forest Labs/ Ironwood Pharmaceuticals' linaclotide (2013 sales US$470 million), AGI Therapeutics' Rezular (2013 sales US$380 million) and Takeda's vedolizumab (2013 sales US$170 million).

Winners & losers

From a company perspective, losers are essentially those companies with large Proton Pump Inhibitors set to face generic competition and sales erosion. Examples include AstraZeneca, Takeda, Wyeth and Nycomed. The size of these products means that companies will be unlikely to offset the sales lost through new product launches in the near-term, though the recent approval of Takeda's Kapidex DR may go some way to limiting the company's exposure to generics.

Winners, on the other hand, are likely to be those companies who have recently launched, or are set to launch, new agents for the treatment of IBD and IBS. Examples include Abbott (with Humira), UCB (with Cimzia), and Biogen Idec/Elan (with Tysabri).

Major Products Evaluated and Forecast to 2013

- **ADX10059**
  (Addex Pharmaceuticals - GORD)
- **Kapidex DR** (dexlansoprazole)
  (Takeda - GORD)
- **linaclotide**
  (Forest Labs/Ironwood Pharmaceuticals - IBS)
- **Rezular** (averapamil)
  (AGI Therapeutics - IBS)
- **vedolizumab** (MLN002)
  (Takeda - IBD)

Answering key business questions...

- What trends are driving growth in the patient populations for acid-related disorders, IBD, IBS and GORD?
- What approaches are being taken in the acid-related disorders market and will they offer any real benefits over current generically-available PPI treatments?
- There are 19 agents in late-stage research for IBS – what therapeutic approaches are being pursued and by which companies?
- What competitive market environment will Takeda's controlled-release GORD treatment Kapidex face when it is launched, and how might that affect sales growth?
- What clinical benefits does Forest Lab' IBS-C treatment linaclotide have, and will they be sufficient to achieve the estimated global sales of US$470 million by 2013?
- When is AGI Therapeutics' novel first-in-class IBS-D treatment Rezular expected to launch, and how might competing product Lotronex's prescribing restrictions help sales growth?

Metabolic

The worldwide prescription metabolic market – comprising obesity and diabetes – was worth US$23 billion in 2007. The market for agents for the treatment of diabetes was worth US$22 billion, divided equally between insulin and non-insulin therapies, while the market for prescription obesity drugs was worth approximately US$1 billion.

Insulin

The insulin market has demonstrated double-digit growth in recent years. This breaks down roughly 50:50 into volume growth (a combined result of the trend towards more intensive therapy and greater patient numbers) and value uplift, as patients switch to new devices and new rapid, long-acting insulin analogues. These trends are expected to continue, albeit at a lower level, over the coming 5 years, and we forecast high single-digit 2008-13 CAGR of 7%. The switch to insulin analogues will continue until about 2011, by which time most suitable patients will have switched and growth will revert to its underlying annual trend of 5-6%.

From a company perspective, we expect the main drivers of growth in the insulin market to be the European players sanofi-aventis and Novo Nordisk, with forecast 2008-13 CAGR for insulin product sales of 11 and 7% respectively, powered by the launch of new insulin analogue products. Eli Lilly, by contrast, after initial market success from the introduction of Humalog, has failed to build on its position.

Non-insulin diabetes agents

Solid growth for non-insulin therapies for the treatment of diabetes is expected, despite the negative impact of generic competition to both Avandia (rosiglitazone) and Actos (pioglitazone) from 2011. Added to this is the adverse impact of the new FDA guidelines for the approval of new agents for the treatment of Type II diabetes (which can add at least 3 years to potential US launch dates). We therefore expect a 2008-13 CAGR of 5% for this market.

From a company perspective, the big losers in the diabetes market are those with agents set to lose patent protection: GlaxoSmithKline and Takeda (though Takeda's declining position in the diabetes market may be offset by the launch of the DPP IV inhibitor alogliptin). Winners are companies such as Merck & Co which has a potential blockbuster on its hands (the DPP IV inhibitor Januvia (sitagliptin)).

Obesity

Despite the growing prevalence of obesity and the unmet need for effective agents, the forecast for 2008-13 CAGR is only 2%. Both Roche's Xenical and Abbott's Meridia have failed to achieve expected sales despite considerable investment, including (in the case of Xenical) the inclusion of data in the label demonstrating a reduction in risk of developing Type II diabetes. New agents in development include Arena's lorcaserin and Shionogi's velneperit.

Major Products Evaluated and Forecast to 2013

- **alogliptin** (SYR 322) *(Takeda - Diabetes)*
- **Byetta LAR** (exenatide) *(Eli Lilly/Amlyn/Alkermes - Diabetes)*
- **dapagliflozin** (BMS-512148) *(BMS/AstraZeneca - Diabetes)*
- **lixisenatide** (AVE0010) *(sanofi-aventis - Diabetes)*
- **lorcaserin** (APD-356) *(Arena Pharmaceuticals - Obesity)*
- **metaglidasen** (MBX-102) *(Johnson & Johnson/Metabolex - Diabetes)*
- **Onglyza** (saxagliptin) *(BMS/AstraZeneca - Diabetes)*
- **velneperit** (S-2367) *(Shionogi - Obesity)*
- **Victoza** (liraglutide) *(Novo Nordisk - Diabetes)*

Answering key business questions...

- Following the termination of Pfizer's Exubera and the suspension of similar products, what is the future for non-injectible insulin?
- Although still in Phase II, hopes are high for Johnson & Johnson/Metabolix's novel Type II diabetes treatment metaglidasen, but issues remain. What are they and what is the potential upside?
- With a superior efficacy and side effect profile to competing Byetta, Novo Nordisk's GLP-1 analogue Type II diabetes treatment Victoza is tipped for success – but what is hindering its commercial development?
- What regulatory and patent obstacles must Arena Pharmaceuticals' 5-HT_{2c} agonist lorcaserin overcome in the troubled obesity market?

Musculoskeletal

The musculoskeletal therapy area is one in which relatively few major patent expiries are expected in the near future. In particular, the rheumatoid arthritis market will demonstrate strong growth, as the greater uptake of new, higher priced, biological therapies progresses. The launch of new agents from Roche/Chugai, Actemra (tocilizumab) and Johnson & Johnson (golimumab) should help bolster growth in this market. The development of new biological therapies targeted at the estimated 30% of patients who do not respond to the TNF blockers, will aid growth.

Rheumatoid arthritis

Despite the introduction of the TNF blockers a decade ago, there remains considerable unmet medical need within the rheumatoid arthritis (RA) market, and it remains an area with a high level of R&D activity with 79 agents under investigation for their potential use in the treatment of the condition. The unmet need is most acute at the more severe end of the disease spectrum, where current products are not only expensive (which has limited their uptake, particularly in Europe), but also associated with unpleasant side effects. Roche has estimated that up to 30% of patients have an inadequate response to the anti-TNF drugs, and recent efforts have focused on developing agents for these patients.

Osteoarthritis

Although the osteoarthritis market is well-served with NSAIDs, many patients do not find these agents sufficient to control their pain, and hence there is always scope in this market for new agents with a good degree of efficacy. In particular, there is an unmet need for new agents with improved gastrointestinal tolerability now that the COX-2 inhibitors are viewed with a degree of caution after the withdrawal of Merck & Co's Vioxx. There are 22 agents under investigation for the treatment of osteoarthritis with many being reformulations of existing products – often with the goal of improving tolerability.

Osteoporosis

Recent years have seen a number of new product introductions for the treatment of osteoporosis, but this remains an area of high unmet medical need, with the need for agents with greater efficacy and tolerability. The most commonly used class of agents, the bisphosphonates, are associated with acid reflux and muscle pain. Additionally, the bisphosphonates are difficult to take: patients are required to fast the night before, remain upright for a period following use, and fast following use. Poor compliance is a primary reason for poor efficacy with this class of agents, and about 50% of patients in a 'real world' setting stop taking bisphosphonates within one year. As a result, a number of alternative approaches are under evaluation and Amgen's RANK Ligand inhibitor has generated a great degree of interest.

Major Products Evaluated and Forecast to 2013

- **Actemra** (tocilizumab) *(Roche/Chugai - Rheumatoid arthritis)*
- **Arzerra RA** (ofatumumab) *(Genmab/GlaxoSmithKline - Rheumatoid arthritis)*
- **denosumab** (AMG162) *(Amgen - Osteoporosis)*
- **Fablyn/Oporia** (lasofoxifene) *(Pfizer/Ligand Pharmaceuticals - Osteoporosis)*
- **golimumab** (CNTO 148) *(Johnson & Johnson/Schering-Plough - Rheumatoid arthritis)*
- **ocrelizumab** (R1594) *(Roche/Genentech/Biogen Idec - Rheumatoid arthritis)*
- **Viviant** (bazedoxifene) *(Wyeth - Rheumatoid arthritis)*

Answering key business questions...

- What impact will generic competition have on the osteoporosis and osteoarthritis markets and which companies will be affected?
- What trends have affected the uptake of TNF blockers and what opportunity does this present for products in the pipeline?
- Why is Roche well placed to achieve commercial success in this sector?
- What advantages does Amgen's first-in-class RANK-L Mab bring to the treatment of osteoporosis and what obstacles will it have to overcome to achieve sales of US$1.45 billion by 2013?
- Will Roche/Chugai's Actemra, be able to challenge TNF blockers and become a first-line treatment for the rheumatoid arthritis market and what could be the commercial rewards?

Oncology

The clear growth driver within the oncology therapeutic area is the continued development and uptake of new targeted agents for the treatment of cancer.

In 2000, of the top ten oncology agents (by sales) worldwide, only one, (Roche/Genentech's Rituxan (rituximab)), was a targeted therapy. By 2010, we estimate that there will only be two non-targeted agents within the top ten by sales (sanofi-aventis' Taxotere (docetaxel) and Roche's Xeloda (capecitabine)). Patent expiries are set to erode sales of the remaining blockbuster chemotherapy and hormonal therapy agents within the next few years, while the new biological agents are benefitting from expanded indications, increased uptake and the lack of a process in the US for the approval of biosimilar agents.

Growth is being driven by targeted therapies

The report forecasts a 2008-13 CAGR for the oncology market of 5%, driven by a forecast 14% CAGR for the targeted therapies sector. Lower growth (a 2008-13 CAGR of 2%) for the chemotherapy class can be expected, as sales of new agents with improved tolerability and/or efficacy are offset by patent expiries on some major agents. Generic competition will erode sales of major products such as sanofi-aventis' Eloxatin (oxaliplatin) and Taxotere and Eli Lilly's Gemzar (gemcitabine) within our forecast period.

Although we expect the emergence of further new targeted cancer therapies to continue to drive sales growth within the oncology market, it is wise to be cautious. Future blockbusters of the size of Roche/ Genentech's VEGF inhibitor Avastin (bevacizumab) may be few and far between in the future, as we expect the market to become increasingly fragmented. The "first mover" advantage in the oncology market is very real, and unless new agents offer a significant advance over existing therapies, oncologists are inclined to stick with what they know. "Me too" agents rarely achieve the sales of the first-to-market.

Winners & losers

In the hormonal therapies category, we expect a 2008-13 CAGR of -7%, as patents expire on several major agents, including AstraZeneca's Zoladex, Casodex and Arimidex, Novartis's Femara and Pfizer's Aromasin.

The other major loser from patent expiries is likely to be sanofi-aventis, which is set to face competition on both Eloxatin and Taxotere.

There will be a number of winners in the oncology market. Roche/Genentech will retain its dominance, and other major players which have strong pipelines in the oncology area include Novartis and AstraZeneca.

Major Products Evaluated and Forecast to 2013

- **Afinitor** (everolimus) *(Novartis - RCC)*
- **aflibercept** (VEGF trap) *(sanofi-aventis/Regeneron - NSCLC, HRPCA, mCRC)*
- **Armala** (pazopanib) *(GlaxoSmithKline - RCC)*
- **Arzerra** (ofatumumab) *(Genmab/GlaxoSmithKline - CLL/NHL)*
- **Bosutinib** (SKI 606) *(Wyeth - CML)*
- **deforolimus** (MK-8669) *(Merck & Co - Metastatic sarcoma)*
- **elesclomol** (STA 4783) *(GlaxoSmithKline/Synta Pharmaceuticals - Metastatic melanoma)*
- **eribulin** (E-7389) *(Eisai - Metatstatic melonoma)*
- **ipilimumab** (MDX010) *(BMS/Medarex - Metastatic melonoma)*
- **pertuzumab** (R 1273) *(Roche - BC)*
- **pixantrone** (BBR-2778) *(Novartis/Cell Therapeutics - NHL)*
- **Zactima** (vandetanib) *(AstraZeneca - NSCLC)*

Answering key business questions...

- Is Wyeth wise to target Novartis' entrenched CML treatment Gleevec (imatinib) with its SRC/ABL kinase inhibitor Bosutinib and what must it do to promote its adoption as a first-line therapy?
- Positive clinical trial results for Roche's HER2/neu dimerisation inhibitor pertuzumab could see it become the standard of care for HER2 positive metastatic breast cancer. But in what other indications might it be clinically valuable?

Respiratory

A modest decline in the value of the respiratory market over the 2008-13 period is expected, with a CAGR of -1%. The asthma market will be responsible for the bulk of this decline in value, with market growth slowing over the 5-year forecast period, then declining from 2012 as the patents on major products such as Merck & Co's Singulair (montelukast) expire. Overall, we forecast a 2008-13 CAGR for the asthma market of -5%.

In the rhinitis market, we also forecast a decline in sales, with a forecast 2008-13 CAGR of -4%, driven by the steady erosion of sales by generic and OTC competition.

There is better news for the Chronic Obstructive Pulmonary Disorder (COPD) sector where growth will offset the declines in sales in asthma and rhinitis. Not only is there continuing growth from the market-leading agent – Boehringer Ingelheim's Spiriva (tiotropium) – but we expect new product launches to also contribute to sales. New product launches from Novartis (indacaterol and glycopyrronium), Nycomed (Daxas), and Almirall/Forest Labs (aclidinium bromide) will power growth over the 2008-13 period, and we forecast a CAGR for this period of 8%. The new product launches will add to growing awareness of the condition, and improve treatment rates, which are currently lower than 50% in many markets.

Asthma

Despite the large size of the asthma market, and the fact that patients in many countries remain under-diagnosed and undertreated, the asthma pipeline currently lacks much in the way of innovative therapies. Hopes for the PDE IV inhibitors were high but their propensity to cause nausea and a relatively narrow therapeutic window have limited their potential. The current focus of late-stage development efforts is the new long-acting beta agonists, which are expected to offer a quicker onset of action, fewer cardiovascular side effects and once daily dosage.

COPD

The main focus of drug development for the treatment of respiratory diseases is in the treatment of COPD – a market which has historically been undertreated and underserved with effective therapies. There is, therefore, considerable market potential, as witnessed by the sales of Boehringer Ingelheim's Spiriva. There are 35 drugs being investigated for their potential in COPD.

Rhinitis

Although the rhinitis market is large in terms of patient numbers, it has attracted relatively little R&D attention in recent years, with new product launches being variations on the antihistamine and intranasal corticosteroid theme. Monoclonal antibodies such as Roche's Xolair have been studied in this indication, but none appear to have progressed as far as a regulatory submission.

Major Products Evaluated and Forecast to 2013

- **aclidinium bromide** (LAS-34273) *(Almirall/Forest Labs - COPD)*
- **Daxas** (roflumilast) *(Nycomed - COPD)*
- **glycopyrronium bromide** (NVA237) *(Novartis - COPD)*
- **indacaterol** (QAB-149) *(Novartis - COPD)*

Answering key business questions...

- What is the value of the global respiratory market?
- There are 300 million asthma and 210 million COPD sufferers worldwide, but COPD only accounts for 20% of the market – why?
- What steps are being taken to improve patient compliance, which is notoriously poor in the respiratory area?
- Why will generic competition have a particularly significant effect on the asthma market?
- Why, despite the need for an effective oral treatment for COPD, might Nycomed's PDE IV inhibitor Daxas fail to achieve its real sales potential?
- Could Novartis' once-daily long-acting muscarinic antagonist, glycopyrronium bromide, unseat Boehringer Ingelheim's Spiriva as the leading COPD product and, if so, what would the commercial benefit be to the company?
- Will Novartis' indacaterol and glycopyrronium bromide be enough to challenge GlaxoSmithKline's domination of the respiratory market?

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