PIPELINE 2010

MM&M takes a detailed look at key products in the pipeline, highlighting the most promising with insights and ratings from top analysts, to provide an overall picture of each therapeutic's potential value

PROVOCATIVE AGENTS

MM&M's Pipeline 2010 draws from the best in drug development, profiling 15 agents with the highest approval probability and brightest commercial prospects. These are the prime near-term launch candidates. The report also provides updates on 202 products in a host of therapeutic areas. **Marc Iskowitz** reports

Qualitative change, rather than the quantitative kind, marks this year's biopharmaceutical pipeline. There has been a shift in categories poised to yield near-term approvals. And while not the goldmine drug marketers were hoping for, analysts expect the 2010 R&D seam to yield some exciting launch prospects in the months and years ahead.

Oncology, a well of innovative approvals in years past, has run relatively dry. "In 2000-2001, we saw Avastin, Tarceva, Sutent, Nexavar, Gleevec—drugs that revolutionized the way we think about treating cancer," notes Ben Weintraub, PhD, director of research, Wolters Kluwer *in*Thought. "The second half of this decade is about using them properly."

Another category making less noise is neurology, with scientists' search for an effective Alzheimer's disease treatment one of the lone highlights. In multiple sclerosis, oral therapy cladribine (Merck/Serono) is set to enter a self-injection and infusion market. Yet analysts see few potential game-changers among Parkinson's disease, schizophrenia, depression or pain candidates.

A cardiovascular blockbuster?

The cardiovascular pipeline, on the other hand, contains a slew of provocative agents that could make a big impact. Indeed, the next blockbuster may be a clot-buster, with Johnson & Johnson and Bayer's Xarelto (rivaroxaban) anticoagulant shaping up to be physicians' best hope to replace warfarin. Then there are the upstarts. Patients with rare diseases are finally getting drugs specifically approved for them. According to a new analysis by the Tufts Center for the Study of Drug Development, the annual rate of new product approvals worldwide for neglected diseases increased from an average of 1.8 in 1975-99 to 2.6 in 2000-09. Vaccines and antiviral drugs have also seen a resurgence, with physicians talking about a possible cure for hepatitis C and a number of vaccines in the pipeline for ailments from flu to cancer and diabetes.

These drug-development dynamics are borne out in *MM&M*'s Pipeline 2010. The report captures the latest trends, profiling 15 agents with a high probability of reaching market and bright commercial prospects. Surveying today's drug-development scene, the report highlights the rare disease and infectious disease categories, along with stalwarts cardiovascular, metabolic and rheumatology. A final category keeps readers updated on neurology, women's health, respiratory and oncology product candidates.

The top picks are based on Wolters Kluwer data. Each profiled drug includes a percentage called the *in*Thought Approvability Index (IAI)—anything above 50% has a good chance—and, where available, a revenue forecast. The IAI uses historical approval rates and detailed analysis of clinical trials to model the probability of approval. Each featured section of the pipeline also includes a box containing additional key products (from Wolters Kluwer data).

Therapeutic Categories:

Cardiovascular

PRODUCTS GENERATING BUZZ

Xarelto (rivaroxaban) Johnson & Johnson/Bayer
Indication: VTE (Prereg.); ACS, stroke prevention (Ph. III)
What the clinical trials found: All four RECORD studies have shown rivaroxaban reduces deep vein thrombosis and pulmonary embolism compared with enoxaparin (Lovenox), with similarly low bleeding rates.
Revenue forecast: $6.8 billion worldwide by 2015, says Craig Maxwell of ING Financial Markets
***in*Thought Approvability Index and Comment:** 95% (VTE), 53% (stroke prevention in AFib). Physicians have been hoping for an oral anticoagulant to replace Coumadin (warfarin) for decades. The implosion of AstraZeneca's factor Xa inhibitor Exanta a few years ago because of safety concerns has left the FDA cautious about approving such agents, but *in*Thought believes that rivaroxaban has a good benefit-risk profile and will be well-accepted by physicians. The drug, already approved in Europe, will be approved in the US first for prophylaxis among patients with venous thromboembolism (VTE). It also has potential in stroke prevention in patients with atrial fibrillation (AFib) and various other clinical scenarios. Estimated approval for VTE in the US: April 2010 (Source: Wolters Kluwer Health).
What the analysts had to say: Physicians are looking for a more convenient and efficacious alternative to warfarin without increased bleed risk. Xarelto, as well as Pradaxa (dabigatran), will meet some of these needs. Both are once-daily, oral and don't require coagulation monitoring, but Xarelto lags Pradaxa for stroke. The FDA's request for data on Xarelto's VTE application is slowing development.
—Mary McBride, Associate VP, GfK Healthcare

Pradaxa (dabigatran) Boehringer Ingelheim
Indication: VTE, stroke prevention (Ph. III)
What the clinical trials found: The RE-LY 18,113-patient phase III trial showed subjects randomized to 150 mg of dabigatran twice a day had significantly lower rates of both hemorrhagic stroke and ischemic stroke than patients taking warfarin.
***in*Thought Approvability Index and Comment:** 67%. Like rivaroxaban, this oral anticoagulant is exciting because of its potential to replace warfarin. Dabigatran's best evidence is for use in patients with atrial fibrillation at risk for stroke, where experts predict it could capture 50% of warfarin's market within five years of approval (Source: Wolters Kluwer Health).
What the analysts had to say: This oral direct thrombin inhibitor is well ahead of agents across classes and should be well-received by physicians for stroke prevention. The RE-LY trial showed promising results, with comparable efficacy to warfarin without increased bleed risk or liver toxicity. Rapid onset of action and lack of coagulation monitoring suggest both physicians and patients will welcome this easier-to-use warfarin alternative.
—Mary McBride, Associate VP, GfK Healthcare

OTHER KEY PRODUCTS IN THE PIPELINE

ABT 335/Crestor Combination Abbott/AstraZeneca
Cholesterol (Ph. III)

Xience V (Bio-Absorbable) Abbott Laboratories
Stent (Ph. III)

Clonidine Addrenex
Hypertension (Prereg.)

Lomitapide Aegerion
Hyperlipoproteinemia type II (Ph. III)

Bucindolol ARCA
Heart failure (Prereg.)

Tecerfarin ARYx
Thromboembolism (Ph. II/III)

YM150 Astellas
Venous thrombosis. (Ph. II/III)

Sematilide Bayer
Arrhythmias (Ph. III)

Cell-based therapies Bioheart
Heart dam. (Ph. III)

Apixaban BMS/Pfizer
ACS, DVT, stroke (Ph. III)

Kynapid (vernakalant) Cardiome/Merck/Astellas
AF acute (Ph. III); maintenance (Ph. II)

Alferminogene Cardium
Myocardia ischem. (Ph. III)

TRIA 662 Cortia
Hyperlipidemia (Ph. II/III)

Diltiazem DOV
Angina, hypertension (Ph. III)

Defibrotide Gentium
Veno-occlusive disease. (Ph. III)

Mipomersen Genzyme
Hyper-cholesterolaemia, -lipoproteinemia type IIa (Ph. III)

Darusentan Gilead
Resistant hypertension (Ph. III)

Darapladib GlaxoSmithKline
Atherosclerosis (Ph. III)

Mepolizumab GlaxoSmithKline
Hypereosinophilic syndrome (Ph. III)

Binodenoson King
Cardiovascular disorders (Prereg.)

Acadesine Merck
Ischem. heart disease. (Ph. III)

Anacetrapib Merck
Atherosclerosis (Ph. III)

Cordaptive Merck
Atherosclerosis (Ph. III)

MK-0524B Merck
Hyperlipidemia (Ph. III); Atherosclerosis (Ph. III)

SCH 530348 Merck
ACS (Ph. III)

Colestilan Mitsubishi
Hyperphosphatemia (Ph. III)

Rolofylline NovaCardia (Merck)
Acute heart failure (Ph. III)

rFXIII Novo Nordisk
Factor XIII defiency (Ph. III)

Azimilide P&G
AF, atrial flutter., supraventricular arrhythmias (Prereg.), arrhythmias, post-MI (Ph. III)

Desmoteplase PAION
Stroke (Ph. III)

MPC 028 URL Pharma
Hyper-cholesterolemia, -lipidemia, -triglyceridemia (Prereg.)

AVE 5026 Sanofi-Aventis
Thromboembolism (Ph. III)

AVE 5530 Sanofi-Aventis
Hypercholesterolema (Ph. III)

Idrabiotaparinux Sanofi-Aventis
Embolism (Ph. III)

Terutroban Servier
Cardiovascular disease (Ph. III)

Azilsartan Takeda
Hypertension (Ph. III)

Xemilofiban VDDI
Cardiovascular disease (Ph. III)

Infectious Disease

PRODUCTS GENERATING BUZZ

Telaprevir Vertex/Johnson & Johnson
Indication: Hepatitis C (Ph. III)
What the clinical trials found: Phase II results showed excellent antiviral activity, offering improved efficacy and reduced duration of treatment vs. conventional therapy.
***in*Thought Revenue forecast:** $1.9 billion US, $2.9 billion worldwide, by 2016
***in*Thought Approvability Index and Comment:** 81%. One of the most exciting drugs in development, telaprevir has been generating exciting results in patients with hepatitis C, with some physicians actually talking about a cure. If approved, this drug would be used in combination with interferon and ribavirin. The most notable adversity to date is a sometimes severe rash. Estimated approval: January 2012 (Source: Wolters Kluwer Health).
What the analysts had to say: Telaprevir, as well as boceprevir (see below), represent new entries in the class referred to as "STAT-Cs," or specifically targeted anti-virals for the treatment of hepatitis C. Physicians are strongly anticipating both. The two are approximately comparable from the standpoint of sustained virologic response in genotype 1 patients. Telaprevir also offers the benefit of a potentially shortened duration of therapy for genotype 1 patients—24 weeks vs. 48. *—Noah Pines, EVP, GfK Healthcare*

Boceprevir Merck
Indication: Hepatitis C (Ph. III)
What the clinical trials found: The phase II HCV SPRINT-1 trial showed that in treatment-naïve patients with HCV genotype 1 infection, a 48-week regimen that included boceprevir 800 mg twice daily resulted in a sustained virological response rate of 75% at 24 weeks, compared with 38% in the control group who received peginterferon alfa-2b + ribavirin alone.
***in*Thought Revenue forecast:** $345 million US, $775 million worldwide, by 2016
***in*Thought Approvability Index and Comment:** 71%. Unfortunately for Merck, boceprevir's profile doesn't appear as exciting as telaprevir's, with slower viral clearance and 50% of patients experiencing anemia. Still, it could become an important new agent for the treatment of hepatitis C. Estimated approval: January 2013 (Source: Wolters Kluwer Health).
What the analysts had to say: Uptake of boceprevir, and fellow HCV protease inhibitor telaprevir, is likely to be robust in both treatment-experienced and naïve patients due to the fact that they offer an increase in efficacy and a potentially abbreviated treatment course (which also suggests an abbreviated duration of treatment-related side effects). They also represent the most significant advantage in HCV therapy since the advent of the pegylated interferons (Peg-Intron from Schering-Plough and Pegasys from Roche).
—Noah Pines, EVP, GfK Healthcare

OTHER KEY PRODUCTS IN THE PIPELINE

Japanese encephalitis vaccine Acambis
Japanese encephalitis (Ph. III)

Sorivudine topical aRigen
Herpes zoster (Ph. II/III)

Apricitabine Avexa
HIV-1 infection (Ph. III)

DR 5001 Barr
Adenovirus infection (Ph. III)

Seasonal influenza virus vaccine Baxter
Seasonal flu (Ph. III)

B cell lymphoma vaccine Biovest/NCI
NHL (Ph. III)

Sipuleucel-T (vaccine) Dendreon
Prostate (ref.) (Prereg.)

Heplisav (hep. B vaccine) Dynavax
HBV infection (Ph. III)

Eritoran Eisai
Gram-neg. infection, septic shock (Ph. III)

PRO 2000 Endo
HIV infection (Ph. III)

Elvitegravir Gilead/Japan Tobacco
HIV-1 infection (Ph. III)

GSK 1572932A GlaxoSmithKline
NSCL (Ph. III)

Inactivated split-trivalent seasonal flu vaccine GlaxoSmithKline
Seasonal flu (Elderly) (Ph. III)

Hib-meningococcal vaccine groups C and Y conj. GlaxoSmithKline
Haemophilus infection (Ph. III); Meningococcal groups C & Y infection (Ph. III)

Ampligen (mismatched double-stranded RNA) Hemispherx
CFS/ME (Prereg.)

Albuferon (albinterferon alfa 2-b) Human Genome Sciences
HCV infection (Ph. III)

Efavirenz/lamivudine/tenofovir disoproxil Matrix
HIV-1 infection (Prereg.)

Motavizumab MedImmune
RSV (Prereg.)

Gardasil (women 27-45) Merck
HPV vaccine (Reg. / Filed)

Vicriviroc Merck
HIV-1 infection (Ph. III)

V503 (vaccine) Merck
HPV infection (Ph. III); Cervical, vulvovaginal cancer (prev.) (Ph. III)

Meningococcal vaccine groups ACY W-135 conj. Novartis
Meningococcal group A, C, Y, W-135 infection (Prereg.)

Tifacogin Novartis
CAP (Ph. III)

West Nile immune globulin OMRIX
West Nile virus infection (Ph. III)

Cancer vaccine BLP25 Oncothyreon/Merck KGaA
Breast cancer, NSCL (Ph. III)

Fidaxomicin/OPT80 Optimer
Clostridium infections (Ph. III)

Pneumococcal vaccine conjugate 13-valent Pfizer
Pneumococcal infection (Prereg.), elderly (Ph. III)

Zithromax/ Chloroquine Pfizer
Malaria (Ph. III)

Influenza virus vaccine Protein Sciences
Influenza virus infection (Prereg.)

Mycophenolate mofetil Roche
Pemphigus vulgaris (Ph. III)

Crofelemer Salix
Diarrhea (Ph. III)

Influenza virus vaccine High Dose Sanofi Pasteur
Influenza virus infection elderly (Prereg.)

Boceprevir Schering-Plough
Hepatitis C (Ph. III)

Vicriviroc Schering-Plough
(HIV Infection) Ph. III

Rilpivirine Tibotec
HIV-1 infection (Ph. III)

Prevnar 13 Wyeth
Invasive pneumococcal disease (Adults & Infants) (Ph. III)

Metabolic

PRODUCTS GENERATING BUZZ

Byetta Once-Weekly (exenatide LAR) Amylin/Lilly/Alkermes
Indication: Type 2 diabetes (Preregistration)
What the clinical trials found: Results of a phase III study (DURATION-1) that included 295 subjects with type 2 diabetes suggest that exenatide LAR may offer improved blood glucose control over marketed Byetta, with similar safety and efficacy.
***in*Thought Revenue forecast:** $1.9 billion US, $3.0 billion worldwide, by 2016
***in*Thought Approvability Index and Comment:** 82%. Byetta is currently approved as a twice-daily injection for patients with type 2 diabetes. Although sales have been flat for three years, *in*Thought expects the once-weekly version to be a success. This formulation should win out over not only the twice-daily Byetta, but also Novo Nordisk's once-daily Victoza (liraglutide). Estimated approval: June 2011 (Source: Wolters Kluwer Health).
What the analysts had to say: Doctors are writing fewer prescriptions for Byetta than in the past, and that may be due to safety concerns with a lot of diabetes meds. Many may be concerned about pancreatitis or are waiting for FDA approval of Byetta LAR. Victoza is expected to arrive on the US market by third-quarter 2010.
—Dave Jacobson, diabetes practice leader/SVP, Roper Diabetes Group, GfK Healthcare

Lorcaserin Arena
Indication: Obesity (Ph. III)
What the clinical trials found: The BLOSSOM phase III study met all primary endpoints and FDA benchmarks over one year. In obese patients treated with 10 mg lorcaserin dosed twice daily, 63% of patients lost at least 5% of their body weight; with 10 mg lorcaserin dosed once daily, 53.1% achieved at least 5% weight loss.
***in*Thought Revenue forecast:** $700 million US, $850 million worldwide, by 2016
***in*Thought Approvability Index and Comment:** 67%. Like Vivus' Qnexa (phentermine/topiramate), lorcaserin is a promising and unpartnered obesity medicine. It has demonstrated less efficacy than Qnexa, but also more mild adversities, a profile that will likely make it more broadly used if approved. Estimated approval: March 2011 (Source: Wolters Kluwer Health).
What the analysts had to say: Lorcaserin efficacy remains modest and with higher rates of SAEs vs. placebo. We continue to believe that regulatory risk persists with data unlikely to support partnership.
—Jim Birchenough, MD, Barclays Capital

Qnexa (phentermine/topiramate) Vivus
Indication: Obesity (Ph. III)
What the clinical trials found: The Ph.III EQUIP study showed once-daily phentermine/topiramate low-dose (3.75 mg/23 mg) and full-dose (15 mg/92 mg) produced a mean weight loss of 5.1% and 11%, respectively, compared to 1.6% in the placebo group.
***in*Thought Revenue forecast:** $425 million US, $525 million worldwide, by 2016
***in*Thought Approvability Index and Comment:** 72%. Although large pharma has shied away from developing obesity medicines lately, several small biotechs have developed promising compounds. Vivus's drug is a combination of two approved agents, phentermine and topiramate. Although likely to be approved, adversities such as cognitive impairment, depression and potential liver concerns are likely to limit use to a subset of obese patients. Estimated approval: August 2011 (Source: Wolters Kluwer Health).

OTHER KEY PRODUCTS IN THE PIPELINE

ALD 101 Aldagen
Metabolic disorders (Ph. III)

Fluoconolone acetonide Alimera/pSivida
Diabetic macular edema (Ph. III)

DiaPep 277 Andromeda
Type 1 diabetes (Ph. III)

AI 401 Autoimmune
Type 1 diabetes (Ph. III)

Dextromethorphan/quinidine Avanir
Emotional lability, diabetic neuropathies (Ph. III)

Dapagliflozin Bristol-Myers Squibb
Type 2 diabetes (Ph. III)

Otelixizumab BTG
Type 2 diabetes (Ph. III)

Diamyd Diamyd Medical
Type diabetes mellitus (Ph. III)

Ranirestat Dainippon Sumitomo
Diabetic neuropathies (Ph. III)

Byetta LAR Eli Lilly
Diabetes (Ph. III)

Ruboxistaurin Eli Lilly
Diabetic retinopathy (Prereg.), Diabetic macular edema (Ph. III)

Teplizumab Eli Lilly
Diabetes (Ph. III)

Insulin oral spray Generex
Type 1 diabetes (Ph. III)

Albiglutide GlaxoSmithKline
Type 2 diabetes (Ph. III)

MK 2866 GTx/Merck
Cachexia (Ph. III)

HPN 100 Hyperion
Hyperammonemia (Ph. III)

Mitglinide Kissei
Type 2 diabetes (Ph. III)

Insulin inhalation Mankind
Type 1, 2 diabetes (Prereg.)

MK-0431C Merck
Diabetes (Ph. III)

Colestilan Mitsubishi Tanabe
Hyperphosphatemia (Ph. III)

Dutogliptin Phenomix
Type 2 diabetes (Ph. III)

Aflibercept Regeneron/Bayer
Age-related macular degen. (Ph. III)

Enclomifene Repros
Hypogonadism (Ph. III)

Taspoglutide Roche
Type 2 diabetes (Ph. III)

Lixisenatide Sanofi-Aventis
Type 2 diabetes (Ph. III)

Tagatose Spherix
Type 2 diabetes (Ph. III)

Alogliptin Takeda
Type 2 diabetes (Prereg.)

Tesamorelin Theratechnologies
Lipodystrophy (Prereg.)

Otelixizumab Tolerx
Type 1 diabetes (Ph. III)

Vitreosolve VitreoRetinal
Diabetic retinopathy (Ph. III)

Rare Disease

PRODUCTS GENERATING BUZZ

Xiaflex (collagenase) Auxilium
Indication: Dupuytren's contracture (Preregistration)
What the clinical trials found: A phase III trial in 35 patients showed local injection achieved a 91% therapeutic success rate for the primary endpoint after ≤ 3 injections compared with a 0% response rate in the placebo group. Adverse events were generally mild to moderate.
***in*Thought Revenue forecast:** $600 million US, $850 million worldwide, by 2016
***in*Thought Approvability Index and Comment:** 96%. Dupuytren's contracture is a rare condition, primarily in the elderly, that causes contraction of the fingers. Xiaflex is likely to become a viable option to surgery for patients not only with Dupuytren's, but also patients with other rare conditions caused by collagen buildup, including frozen shoulder syndrome and peyronie's disease. Estimated approval: Dec. 15, 2009 (Source: Wolters Kluwer Health).
What the analysts had to say: Xiaflex is injectable, so safety profile issues are almost nonexistent. We are picking up on a lot of interest from hand surgeons who use it—they say it will cut into their business. *—Ben Weintraub, PhD, director of research, Wolters Kluwer inThought*

DX-88 Dyax
Indication: Hereditary angioedema (HAE) (Preregistration)
What the clinical trials found: Phase III data showed significant improvements in the severity of an HAE attack compared with placebo and good tolerability.
Revenue forecast: $165 million worldwide by 2014, says Phil Nadeau of Cowen + Co.
***in*Thought Approvability Index and Comment:** 90%. Although HAE is a rare condition, several drugs are vying for approval and use. *in*Thought believes that Dyax's DX-88 is the most promising. Others include Viropharma's approved drug Cinryze, CSL Behring's Berinert (approved this year), Pharming's Rhucin and Shire's icatibant. Estimated approval date: December 15, 2009 (Source: Wolters Kluwer Health).
What the analysts had to say: The two approved HAE therapies are C1-INH inhibitors taken prophylatically. What doctors and patients really want is something that can be put in the medicine chest and administered when an HAE attack is coming on. *—Ben Weintraub, PhD, director of research, Wolters Kluwer inThought*

OTHER KEY PRODUCTS IN THE PIPELINE

Masitinib AB Science
Mastocytosis (Ph. III)

Ethyl eicosapentaenoic acid Amarin
Huntington's disease (Ph. III)

Migalastat Amicus/Shire
Fabry's disease (Ph. III)

AT1001 Amicus
Fabry's disease (Ph. II)

AT2101 Amicus
Gaucher's disease (Ph. II)

AT2220 Amicus
Pompe disease (Ph. II)

PEG-PAL Biomarin
PKU (Ph. II)

Corticorelin Celtic Pharma
Brain edema (Ph. III)

Ataluren Genzyme
Cystic fibrosis (Ph. III); Duchenne and Becker muscular dystrophy (Ph. II)

Genz-112638 oral therapy Genzyme
Gaucher's disease (Ph. III)

Thymoglobulin Genzyme
Myelodysplastic syndromes (Ph. II)

TSH Genzyme
Nontoxic multinodular goiter (Ph. II)

Dimebolin Medivation/Pfizer
Huntington's disease (Ph. III)

Amantadine Recordati
Huntington's disease (Ph. III)

Idebenone Santhera
Duchenne muscular dystrophy (Ph. III)

HGT-2310 Shire
Hunter syndrome (Ph. II)

HGT-1111 Shire
Metachromatic leukodystrophy (Ph. III)

Firazyr Shire
HAE (Ph. III)

Velaglucerase alfa Shire/Protalix
Gaucher's disease type 1 (Prereg.)

Krystexxa (pegloticase) Savient
Indication: Gout (Preregistration)
What the clinical trials found: Primary data from two phase III trials in patients with treatment-failure gout showed clinically meaningful improvements and good tolerability.
***in*Thought Approvability Index and Comment:** 90%. Although gout is a common condition, treatment refractory gout is an orphan indication. Xiaflex is one of two new gout drugs (Takeda's Uloric was approved this year) that is likely to significantly improve the outlook for patients with severe gout. Estimated approval: August 2010 (Source: Wolters Kluwer Health).
What the analysts had to say: We think this will be very successful, but the treatment-refractory population is small.
—Geoff Penney, VP, GfK Healthcare
Validation of Krystexxa batches is progressing well, and FDA-related label and REMS discussions continue to suggest a broad and unrestrictive market opportunity in treatment-failure gout.
—Salveen Kochnover, CFA, Collins Stewart

Rheumatology

PRODUCTS GENERATING BUZZ

Prolia (denosumab) Amgen
Indication: Osteoporosis (Preregistration); bone discorders cancer, (Ph. III)
What the clinical trials found: Phase II studies in patients with advanced cancers have shown that denosumab is as effective as IV bisphosphonates at suppressing the ratio of bone turnover markers, with more rapid, sustained absorption and consistent adverse events.
***in*Thought Revenue forecast:** $1.8 billion US, $2.9 billion worldwide, by 2016
***in*Thought Approvability Index and Comment:** 96%. Probably the most exciting developmental drug of 2009, Prolia is a rank-ligand inhibitor that will compete with bisphosphonates for the treatment of osteoporosis and in some cancer scenarios. *in*Thought expects Prolia will be approved early next April and become a blockbuster. (Source: Wolters Kluwer Health).
What the analysts had to say: As the first biologic in the osteoporosis space, denosumab is expected to provide significant efficacy. The clinical trials seem to bear that out. Based on what we know about other biologics, this one will be cautiously adopted by physicians given the risk profile.
—Geoff Penney, VP, category business leader, GfK Healthcare

Benlysta (belimumab) Human Genome Sciences/GSK
Indication: Systemic lupus erythematosus (Ph. III)
What the clinical trials found: Treatment of 10 mg/kg in addition to standard care resulted in a significant improvement in patient response after 52 weeks, compared with placebo plus standard of care, meeting the primary endpoint in the phase III BLISS-76 trial.
Revenue forecast: Peak sales of at least $3 billion, says Jim Birchenough of Barclays Capital
***in*Thought Approvability Index and Comment:** 66%. Drug development for lupus has been littered with failures, but Human Genome's drug is on track. The anti-BLyS antibody showed exceptionally strong results from its first phase III trial. Although data from a second phase III trial were somewhat mixed, FDA filing should remain on track for early 2010 (Source: Wolters Kluwer Health).
What the analysts had to say: While off-label use of currently available biologics may erode opportunities, I don't think it will as Benlysta will have the power of promotion, thanks to GSK's marketing muscle.
—Geoff Penney, VP, category business leader, GfK Healthcare

CP 690,550 Pfizer
Indication: Rheumatoid arthritis (Ph. III)
What the clinical trials found: Two six-month phase IIb studies showed rapid and sustained improvement in pain, physical functioning, fatigue and health-related quality-of-life parameters.
***in*Thought Comment:** Physicians and patients are excited about the potential to replace injectable drugs for severe RA with an oral pill. Pfizer's JAK kinase inhibitor is the lead drug with such potential. Phase III results presented at October's American College of Rheumatology meeting are very promising (Source: Wolters Kluwer Health).
What the analysts had to say: This JAK-inhibitor has a unique mode of action and will be one of the first oral therapies in the RA market. (The biologics are all self-injection or infusion therapies.) It's going to be interesting to see how quickly patients demand oral therapies and physicians oblige.
—Geoff Penney, VP, category business leader, GfK Healthcare

OTHER KEY PRODUCTS IN THE PIPELINE

Tissue repair stem cell therapy Aastrom Biosciences
Osteonecrosis (Ph. III)

ABT-874 Abbott
Inflammation (Ph. III), Plaque psoriasis (Ph. III)

Masitinib AB Science
Gastro. stromal disorders, pancreatic cancer (Ph. III)

Laquinimod Active Biotech
MS (Ph. III)

Oral dnaJP1 Adeona
RA (Ph. III)

Interferon-alpha Amarillo/Hayashibara
Sjogren's syndrome (Ph. III)

Esomeprazole/naproxen AstraZeneca/Pozen
Ankylosing spondylitis, osteoarth., RA (Prereg.)

BG 12 Biogen Idec
MS (Ph. III)

PEG-interferon B-1a Biogen Idec
MS (Ph. III)

Ocrelizumab Biogen Idec/Roche
Lupus nephritis, RA (Ph. III)

Belatacept Bristol-Myers Squibb
Renal transplant rej. (Prereg.)

Fampridine SR Elan
MS (Prereg.)

Prasterone Genelabs
Systemic lupus erythematosus (Ph. III)

Alemtuzumab Genzyme
MS (Ph. III)

Hectorol Genzyme
Psoriasis (Ph. II)

Prochymal Genzyme
Crohn's disease, GVHD (Ph. III)

Thymoglobulin Genzyme
Liver transplant (Ph. II)

Epratuzumab Immunomedics/UCB
Systemic lupus erythematosus (Ph. III)

Alicaforsen Isis
Pouchitis, ulcerative colitis (Ph. III)

Voclosporin Isotechnika
Plaque psoriasis, uveitis (Ph. III)

MK-0822 (odanacatib) Merck
Osteoporosis (Ph. III)

Fingolimod Novartis
MS (Ph. III)

Naproxinod NicOx
Osteoarthritis (Prereg.)

Fingolimod Novartis
MS (Ph. III)

Omr-IgG-am OMRIX
Immunodeficiency disorders (Ph. III)

Prochymal Osiris
Crohn's disease, GVHD (Ph. III)

S,S-Reboxetine Pfizer
Fibromyalgia (Ph. III)

Ataluren PTC/Genzyme
Cystic fibrosis (Ph. III)

Mycophenolate mofetil Roche
MS (Ph. II/III)

Beclometasone oral Soligenix
GVHD (Prereg.)

Other

PRODUCTS GENERATING BUZZ

Cladribine tablets Merck Serono
Indication: Multiple sclerosis (Preregistration)
What the clinical trials found: A clear effect on neurological functioning was seen in a two-year crossover study in 24 pairs of disease-matched patients with chronic MS.
***in*Thought Revenue forecast:** $150 million US, $350 million worldwide, by 2016
***in*Thought Approvability Index and Comment:** 76%. Injectable cladribine has been approved for many years as a cancer drug, but now oral cladribine is looking promising as a therapy for multiple sclerosis. Patients and physicians are excited about the potential of an oral medicine that can replace injectable interferons and Copaxone in MS treatment, but most experts believe that it will be a long time before cladribine and other oral drugs are used as first-line MS therapy. Estimated approval: June 2010 (Source: Wolters Kluwer Health).
What the analysts had to say: The physician-patient dynamic will be extremely interesting to watch. Neurologists are typically conservative in terms of medication decisions, and oral cladribine has some risk factors. We are anxious to see the reaction among MS patients, who are highly knowledgeable about treatment options and accustomed to taking risk with their current medications.
—Geoff Penney, VP, GfK Healthcare

Gammagard (immune globulin) Baxter
Indication: Alzheimer's disease (Ph. III)
What the clinical trials found: In a six-month phase II study, Gammagard was associated with significant clinical benefits in patients with AD, with findings indicative of potential efficacy and tolerability.
***in*Thought Revenue forecast:** $1.6 billion US, $3.0 billion worldwide, by 2016
***in*Thought Approvability Index and Comment:** 55%. Gammagard is notable for being the only AD drug that has a greater than 50% probability of approval in the *in*Thought models. Other phase III drugs, most notably Elan/Wyeth's bapineuzumab, have significant challenges to overcome. Still, any successful disease modifying Alzheimer's drug would have a major impact on patient care. Gammagard is interesting because intravenous immunoglobulin has been approved for many years for the treatment of conditions such as reducing the risk of transplant rejection. Estimated approval: September 2012 (Source: Wolters Kluwer Health).
What the analysts had to say: The big challenges are expected to be cost and availability of the medication, as Gammagard is derived from human plasma donors.
—Geoff Penney, VP, GfK Healthcare

OTHER KEY PRODUCTS IN THE PIPELINE

NEUROLOGY

Pimavanserin ACADIA
Psychotic disorders (Ph. III)

Almorexant Actelion/GSK
Insomnia (Ph. III)

Nalmefene Biotie/Lundbeck
Alcoholism (Ph. III)

Lurasidone Dainippon Sumitomo
Bipolar disorder (Ph. III)

CPI 300 IntelGenx/Cary
Depression (Prereg.)

Neramexane Merz
Tinnitus (Ph. III)

Dimebolin Medivation/Pfizer
Alzheimer's disease (Ph. III)

Indiplon Neurocrine Biosciences
Insomnia (Prereg.)

Esmirtazapine Organon
Insomnia (Ph. III)

Carisbamate Ortho-McNeil
Epilepsy (Prereg.)

Vilazodone PGxHealth
Depression (Ph. III)

Eplivanserin Sanofi-Aventis
Insomnia (Prereg.)

Tasimelteon Vanda
Insomnia (Ph. III)

RESPIRATORY

Pollinex Quattro Allergy Thera.
Seasonal allergic rhinitis (Ph. III)

Grass pollen allergy vaccine Artu Biologicals
Seasonal allergic rhinitis (Prereg.)

Reslizumab Ception
Oesophagitis (Ph. III)

Sinapultide Discovery Labs
Neonatal resp. distress synd. (Prereg.)

Aclidinium bromide Forest/Almirall
COPD (Ph. III)

Ragweed allergy vaccine Greer
Seasonal allergic rhinitis (Ph. III)

Denufosol Inspire
Cystic fibrosis (Ph. III)

Loratadine/ montelukast Merck
Seasonal allergic rhinitis (Ph. III)

Mometasone/formoterol Merck
Asthma (Prereg.), asthma, COPD (Ph. III)

Indacaterol Novartis/Skye
COPD (Prereg.), asthma (Ph. III)

Roflumilast Nycomed
COPD (Prereg.), asthma (Ph. III)

Flutiform SkePharma
Asthma (Prereg.)

ONCOLOGY

Motesanib Amgen/Millennium
NSCL (Ph. III)

Cediranib AstraZeneca
Colorectal (Ph. III)

Vandetanib AstraZeneca
Thyroid (Ph. III)

Zibotentan AstraZeneca
Prostate (Ph. III)

Pixantrone Cell Therapeutics
NHL (Prereg.)

Omacetaxine mepesuccinate Chemgenex/Stratagem
CML (Prereg.)

Exatecan Daiichi-Sankyo
Pancreatic (Ph. III)

Oblimersen Genta
CLL (Prereg.), AML (Ph. III)

Odanacatib Merck
Bone cancer (Ph. III)

Motexafin Pharmacyclics
Brain (Prereg.)

Oregovomab Quest Therapeutics
Ovarian (Ph. III)

Larotaxel Sanofi-Aventis
Pancreatic (Ph. III)

BSI 201 Sanofi-Aventis
Breast (Ph. III)

Cabazitaxel Sanofi-Aventis
Prostate (Ph. III)

Laromustine Vion
AML (Prereg.)

Triacetyluridine Wellstat
Pancreatic (Ph. III)

WOMEN'S HEALTH

Flibanserin Boehringer Ingelheim
Female sexual dysfunction (Ph. III)

Cositecan Bionumerik
Ovarian cancer (Ph. III)

Farletuzumab Morphotek
Ovarian cancer (Ph. III)

Patupilone Novartis
Ovarian cancer (Ph. III)

Esmirtazapine Organon
Vasomotor symptoms (Ph. III)

Corifollitropin alfa Organon
Infertility (Ph. III)

Ospemifene QuartRx
Vaginal atrophy (Ph. III)

Tirapazamine SRI
Cervical cancer (Ph. III)