

PIPELINE 2011 LAUNCH PROSPECTS

MM&M's Pipeline 2011 offers a short list of the so-called locks and long-shots to reach market over the next months and years. You'll find details on 14 specific late-stage candidates, selected based on their potential for approval or impact, along with nearly 200 other therapeutics. **Marc Iskowitz** reports

Pharma and biotech companies are hoping for a recovery in R&D productivity to replace aging blockbusters. But any rebound in new product approvals will have to wait until the research drought is over. It's as hard as ever to find agents near launch that might make a commercial impact.

That's not for a lack of effort. "[The pipeline] is chock full of phase III studies, but that's always been the case," says Ben Weintraub, PhD, director of research, Wolters Kluwer *inThought*. "The question is, why haven't we had any blockbusters in the last few years?"

Reaching late-stage development—as all of these candidates have—is a good start. This report includes a number of important, novel therapies pegged by most analysts to reach blockbuster level—industry parlance for \$1 billion in sales—and some wild cards worth watching.

Among the blue-chip launch prospects are two for treating patients with malignant melanoma: ipilimumab, the Bristol-Myers Squibb monoclonal antibody, and PLX 4032, the Roche/Plexxikon BRAF inhibitor. And much as Bayer's Nexavar, Pfizer's Sutent and Roche/Genentech's Avastin altered the outlook in renal cancer, Weintraub predicts these experimental agents will do the same for skin cancer.

Locks and long-shots

In the metabolic category, a new oral class of diabetes meds is gaining steam, the SGLT2 inhibitors. There's also an inhalable insulin, MannKind's Afrezza, that some say has an outside chance, if FDA

concerns over lung safety can be assuaged. And don't count out obesity. Seeing as the agency rejected Arena's lorcaserin and Vivus' Qnexa weight-loss hopefuls in October, will Orexigen's Contrave have the right mix of safety and efficacy to satisfy regulators?

Another long-shot, but one with huge potential, hails from the cardiovascular area. With anacetrapib—a molecular cousin of Pfizer's failed torcetrapib—Merck hopes to realize the promise of the CETP inhibitor class in atherosclerosis.

Finally, two holdovers from last year's Pipeline Report, the hepatitis C therapies telaprevir and boceprevir, have analysts crowing. They say data released over the past year have narrowed differences between the two promising drugs, and that's good for patients. Standouts from the infectious disease, oncology, metabolic and cardiovascular areas are joined by those from rheumatology, plus a separate page with short lists covering respiratory, women's health, neurology and rare disease.

Top picks are based on consultation with Wolters Kluwer *inThought* and other experts. Since any close call is a mere bounce away from becoming a near miss, profilees include, in addition to the expected approval date, an *inThought* Approvability Index—a percentage to help readers gauge the likelihood of an FDA OK based on the agent's safety and efficacy through each phase of clinical development; anything above 50% has a good chance. Add in clinical trial results, analyst comment, revenue forecasts and extensive lists of other key products, and you get a pretty good overview of the late-stage biopharmaceutical drug pipeline.

THERAPEUTIC CATEGORIES:

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Cardiovascular

PRODUCTS GENERATING BUZZ

Brilinta (ticagrelor) AstraZeneca

Indication: Reducing thrombotic events in patients with heart attacks (Prereg.)

What the clinical trials found: The PLATO phase III study showed ticagrelor reduced CV death, myocardial infarction or stroke by 16% compared to the market leader, Bristol-Myers Squibb/Sanofi-Aventis' once-daily Plavix (clopidogrel).

inThought Approvability Index and Comment: 97%. This twice-daily, oral blood thinner is very much like Eli Lilly/Daiichi Sankyo's Effient. Although Effient has been a disappointment, we think Brilinta is going to be quite good and could very well be accepted by cardiologists, as AZ has done a very good job defining who should use Brilinta instead of Plavix, and that has been a problem for Effient. In July an FDA panel gave Brilinta thumbs up, but the agency extended the review time due to side effects—ventricular pauses and shortness of breath. Estimated approval: January 2011 (Source: Wolters Kluwer Health).

Revenue forecast: \$900 million in worldwide revenue by 2015, says Tim Anderson of Bernstein Research

What the analysts are saying: Reversible platelet recovery is faster with Brilinta than with Effient. This, as well as long-term CV protection in patients who have sustained a heart attack (which AZ is now studying) could be key differentiators in the marketplace, especially once Plavix goes generic in May 2012. —*Portia Gordon, assoc. VP, GfK HealthCare*

Anacetrapib Merck

Indication: Atherosclerosis (Phase III)

What the clinical trials found: A phase IIb study of this HDL-cholesterol raising drug showed a very healthy increase in HDL, coupled with a good reduction in LDL.

inThought Approvability Index and Comment: 55%. The best mechanism for HDL-raising has yet to be hashed out, but CETP inhibition remains an exciting possibility. At press time, Merck was slated to release data from a phase III trial looking at efficacy and safety. The primary endpoint will be change in lipid levels, but many will be watching for a trend in CV events. A phase III trial to determine whether adding anacetrapib to a statin reduces the risk of death and heart attacks—the same trial that scuttled Pfizer's torcetrapib four years ago—is set to start in 2011. Estimated approval: April 2012 (Source: Wolters Kluwer Health).

inThought Revenue forecast: If it works, huge

What the analysts are saying: While CETP inhibition is promising, it remains to be seen whether it is a viable strategy. I am not as excited about this mechanism of action, in terms of treating coronary artery disease, as I am about Brilinta, because anacetrapib is entering a very crowded market and has to be able to stand out against other tried and true agents—statins, fenofibrates, beta blockers and

OTHER KEY PRODUCTS IN THE PIPELINE

Stedivaze (apadenoson) Adenosine Therapeutics
Coronary disorders (Ph. III)

Sensipar (cinacalcet) Amgen
Cardiovascular disorders (Ph. III)

Gencaro (bucindolol) ARCA Heart failure (Prereg.)

Certriad (rosuvastatin + choline fenofibrate) AstraZeneca/Abbott
Hyperlipidemia (Prereg.)

Terutroban sodium Boston University Thromboembolism (Ph. III)

Apixaban BMS/Pfizer Stroke preven. in AFib., VTE (Ph. III)

Generx (alferminogene tadenovec) Cardium Therapeutics
Myocardial ischemia (Ph. III)

Droxidopa Chelsea Therapeutics
Orthostatic hypotension (Ph. III)

Human prothrombin complex CSL Behring Hemorrhage (Ph. III)

Varespladib Eli Lilly
Acute coronary syndromes (Ph. III)

Mipomersen Genzyme
Hypercholesterolemia (Ph. III)

Darapladib GlaxoSmithKline
Atherosclerosis (Ph. III)

Parogrelil Indigo Pharmaceuticals
Intermittent claudication (Ph. III)

Xarelto (rivaroxaban) Johnson & Johnson DVT, thromboembolism (Prereg.)

Desmoteplase Lundbeck/Paion
Stroke (Ph. III)

Kynapid (vernakalant) Merck/Cardiome Atrial fibrillation (Prereg.)

MK-0524A (ER niacin/laropiprant) Merck Atherosclerosis (Ph. III)

MK-0524B (ER niacin/laropiprant/simvastatin) Merck
Atherosclerosis (Ph. III)

Vorapaxar/SCH 530348 Merck
Thrombosis (Ph. III)

LCZ 696 Novartis Heart failure (Ph. III)

RLX030 Novartis
Acute heart failure (Ph. III)

Tafamidis meglumine Pfizer
Cardiomyopathies (Ph. III)

Dalcetrapib/RG1658 Roche
Atherosclerosis (Ph. III)

AVE5026 Sanofi-Aventis
VTE prevention (Ph. III)

Otamixaban Sanofi-Aventis
Acute coronary syndromes (Ph. III)

Semuloparin Sanofi-Aventis
Thromboembolism (Ph. III)

Temusi/NV1FGF Sanofi-Aventis
Ischemia (Ph. III)

Irbesartan Shionogi
Hypertension (Ph. III)

Defibrotide Sigma Tau DVT (Ph. III)

Azilsartan Takeda
Hypertension (Prereg.)

Azilsartan kamedoxomil chlortalidone Takeda
Hypertension (Ph. III)

Azimilide Warner Chilcott
Arrhythmias (Ph. III)

antihypertensives—which are not without their own adverse events but are being used. In addition, it still remains to be proven that CETP inhibition affords protection against atherosclerotic disease. —*Portia Gordon, assoc. VP, GfK HealthCare*

Infectious Disease

PRODUCTS GENERATING BUZZ

Telaprevir **Vertex/Johnson & Johnson**

Indication: Hepatitis C (Phase III)

What the clinical trials found: In the phase III ADVANCE study, about 70% of treatment-naïve patients achieved a cure (not including relapsers or non-responders). That and shorter treatment duration—24 vs. 36 weeks—may offer telaprevir an edge over boceprevir (see below).

inThought Approvability Index and Comment: 87%. Doctors are reportedly saying that, on the first day it's available, they will give telaprevir to every one of their hepatitis C patients. This is an add-on to the current standard of care but one that can shorten duration from one year to six months. Estimated approval: January 2012 (Source: Wolters Kluwer Health).

inThought Revenue forecast: \$2.3 billion worldwide by 2018

What the analysts are saying: Telaprevir is a little more efficacious than boceprevir, and will be administered for a shorter period of time than boceprevir. Some KOLs indicate that this latter differentiation point might spoil boceprevir's success, enabling telaprevir to gain more market share.

—Dr. Alexandra Makarova, analyst, Decision Resources

Boceprevir **Merck**

Indication: Hepatitis C (Phase III)

What the clinical trials found: The SPRINT-2 phase III trial showed a cure rate of 66% for the longer duration, 63% for the shorter duration, among treatment-naïve patients.

inThought Approvability Index and Comment: 80%. Boceprevir has almost exactly the same efficacy as telaprevir (see above) but is a little less safe. Differences are narrowing, so we expect them both to be successful, although safety will hamper boceprevir's uptake. We surveyed 75 doctors, and they preferred telaprevir by nearly 2:1. Estimated approval: August 2012 (Source: Wolters Kluwer Health).

inThought Revenue forecast: \$931 million worldwide by 2018

What the analysts are saying: While the drug is likely approvable, its efficacy may be slightly less than that of telaprevir and it will have to be administered longer. The question is whether Merck's marketing muscle can overcome fewer product attributes. Physicians who can pinpoint patients' susceptibility to skin problems may choose to start them on boceprevir because it's more notorious for anemia than rash, which has been telaprevir's main side effect. Due to this difference in side effect profiles, physicians might also choose to prescribe telaprevir rather than boceprevir for patients who have a high chance of developing anemia

—Dr. Alexandra Makarova, analyst, Decision Resources

OTHER KEY PRODUCTS IN THE PIPELINE

MEDI-3250 **AstraZeneca**

Seasonal influenza vaccine, quadrivalent (Ph. III)

Motavizumab **AstraZeneca**

Respiratory syncytial virus prevention (Prereg.)

Numax (motavizumab) **AstraZeneca**

Respiratory syncytial virus infections (Prereg.)

Preflucel (vaccine) **Baxter**

Influenza virus infections (Ph. III)

Peramivir **BioCryst**

Influenza virus infections (Ph. III)

Belatacept **Bristol-Myers Squibb**

Renal transplant rejection (Prereg.)

Varicella zoster immune globulin **Cangene**

Varicella zoster virus infections (Ph. III)

Heplisav **Dynavax**

Hepatitis B (Ph. III)

Nuvocid (oritavancin) **Eli Lilly/Targanta**

Gram pos., skin and soft tissue infections (Ph. III)

Elvitegravir **Gilead**

HIV-1 infections (Ph. III)

Elvitegravir/emtricitabine/tenofovir disoproxil fumarate/GS 9350 **Gilead Sciences**

HIV-1 infections (Ph. III)

Emtricitabine/rilpivirine/tenofovir disoproxil fumarate **Gilead Sciences**

HIV-1 infections (Ph. III)

Diphtheria tetanus pertussis-hepatitis B vaccine **GSK**

(Ph. III)

Mosquirix (vaccine) **GlaxoSmithKline**

Malaria prophylaxis (Ph. III)

Nimenrix **GlaxoSmithKline**

Meningococcal inf. (children) (Ph. III)

MenHibrix (vaccine) **GlaxoSmithKline**

Meningococcal groups C, Y inf., hemophilus inf. (Prereg.)

New generation flu vacc. **GlaxoSmithKline**

Seasonal influenza (Ph. III)

Influenza virus vaccine **GSK**

2186877A **GlaxoSmithKline**

Influenza virus infections (Ph. III)

Simplirix **GlaxoSmithKline**

Genital herpes prophylaxis (Ph. III)

Flu pandemic & pre-pandemic **GSK**

Pandemic H5N1 influenza prophylaxis (Prereg.)

ABthrax (raxibacumab) **Human Genome Sciences**

Anthrax (Prereg.)

Doribax (doripenem) **Johnson & Johnson**

Nosocomial pneumonia (Prereg.)

TMC278 (rilpivirine) **Johnson & Johnson**

NNRTI HIV/AIDS (Prereg.)

MK-3009 (daptomycin) **Merck**

Staph infection (Ph. III)

V503 **Merck**

HPV infections (Ph. III)

PTK796 (omadacycline) **Novartis**

cSSSI (Ph. III)

Optafu influenza virus vaccine **Novartis**

Influenza virus infections (Prereg.)

Fidaxomicin **Optimer Therapeutics**

Clostridium infections (Prereg.)

Prulifloxacin **Optimer Therapeutics**

Gram pos./neg. inf., traveller's diarrhea (Ph. III)

Moxidectin **Pfizer**

River blindness (Ph. III)

Pprevnar 13 adult **Pfizer**

Infectious pneumococcal vaccine (Ph. III)

FluBlok (vaccine) **Protein Sciences**

Influenza virus infections (Prereg.)

ChimeriVax-JE **Sanofi Pasteur**

Japanese encephalitis vaccine (Ph. III)

Fluzone ID (vaccine) **Sanofi Pasteur**

Influenza virus infections (Prereg.)

Adacel (vaccine) **Sanofi Pasteur**

Diphtheria (Ph. III)

Metabolic

PRODUCTS GENERATING BUZZ

Dapagliflozin **Bristol-Myers Squibb/AstraZeneca**

Indication: Type 2 diabetes (Phase III)

What the clinical trials found: A phase III study of this once-daily oral antidiabetic demonstrated significant reduction in HbA1c in patients with newly diagnosed type 2 diabetes, compared to placebo, but also a link to urinary tract infections (UTIs).

inThought Approvability Index and Comment: 40%. SGLT2 inhibitors represent a new class that allows the kidneys to pick up glucose and expel it in the urine. But this molecule is not heading in the right direction. Approvability dropped from 58% to 40% because of more phase III data on UTIs and back pain. Estimated approval: June 2012 (Source: Wolters Kluwer Health).

inThought Revenue forecast: \$1.4 billion worldwide by 2017

What the analysts are saying: Only about one in 10 diabetes patients reports some kind of kidney difficulty. That would suggest a pretty good opportunity, especially as the drug reduces A1cs and offers other benefits, such as reduced incidence of hypos and potential weight loss. — *David Jacobson, diabetes practice leader, GfK HealthCare*

Afrezza **MannKind**

Indication: Types 1 and 2 diabetes (Prereg.)

What the clinical trials found: A phase III study showed no difference in pulmonary function vs. standard insulin therapy.

inThought Approvability Comment: Afrezza will never get approved. We haven't seen very much data, and the bar for a drug that's just replacing another drug, which does the same thing and is known to be safe, is very high. Even if approved, we haven't found any excitement around the physician community (Source: Wolters Kluwer Health).

What the analysts are saying: Afrezza is an especially rapid-acting insulin expected to go up against Eli Lilly's Humalog and Sanofi-Aventis' Apidra. If MannKind can help HCPs get around the insulin stigma, that will certainly benefit the patients for whom insulin is an option. Early next year, things should get very interesting for MannKind, assuming the end-of-year PDUFA date is met by the FDA. — *David Jacobson, diabetes practice leader, GfK HealthCare*

Contrave (bupropion + naltrexone) **Orexigen Therapeutics/Takeda**

Indication: Obesity (Prereg.)

What the clinical trials found: A phase III trial of this combination antidepressant/addiction treatment pill showed weight loss in the 6% range.

inThought Approvability Index and Comment: 72%. Contrave has the highest approval probability in our model, not because its rating has gone up but because of a loss of momentum by the other two investigational obesity compounds—Arena/Eisai's lorcaserin and Vivus' Qnexa, both rejected by FDA in October. An FDA panel is scheduled to vote on Contrave on December 7, with the PDUFA date January 31. Estimated approval: March 2011 (Source: Wolters

OTHER KEY PRODUCTS IN THE PIPELINE

Bydureon (exanatide LAR)

Alkermes/Amylin/Eli Lilly
Type 2 diabetes (Prereg.)

DiaPep 277 **Andromeda Biotech/ Teva Pharmaceuticals**

Type 1 diabetes (Ph. III)

Linjeta (injectable insulin) **Biodel**

Type 1,2 diabetes (Ph. III)

Ondero (linagliptin) **Boehringer Ingelheim**

Type 2 diabetes (Ph. III)

Dapagliflozin/metformin **Bristol-Myers Squibb**

Type 2 diabetes (Ph. III)

Saxagliptin/metformin **BMS**

Type 2 diabetes (Prereg.)

Ranirestat **Eisai**

Diabetic neuropathies (Ph. III)

Mitiglinide **Elixir Pharma**

Type 2 diabetes (Ph. III)

Insulin oral **Generex Biotechnology**

Type 1 diabetes (Ph. III)

Otelixizumab **GlaxoSmithKline**

Type 1 diabetes (Ph. III)

Syncria (albiglutide) **Human Genome Sciences/GSK**

Type 2 diabetes (Ph. III)

Autoimmune diabetes vaccine

Ortho-McNeil-Janssen
Type 1 diabetes (Ph. III)

Canagliflozin **Johnson & Johnson**

Type 2 diabetes (Ph. III)

GAD65 **Johnson & Johnson**

Type 1 diabetes (Ph. III)

LY 2189265 (GLP-1 Fc) **Eli Lilly**

Type 2 diabetes (Ph. III)

Sitagliptin/pioglitazone **Merck**

Type 2 diabetes (Ph. III)

Sitagliptin/simvastatin **Merck**

Type 2 diabetes (Ph. III)

Insulin degludec **Novo Nordisk**

Type 1,2 diabetes (Ph. III)

Lixivaptan **Pfizer**

Hyponatremia (Ph. III)

Dutogliptin **Phenomix**

Type 2 diabetes (Ph. III)

Alelitazar/RG1439 **Roche**

Type 2 diabetes (Ph. III)

Lixisenatide **Sanofi-Aventis**

Type 2 diabetes (Ph. III)

Tagatose **Spherix**

Type 2 diabetes (Ph. III)

Aalogliptin **Takeda**

Type 2 diabetes (Prereg.)

Aalogliptin metformin **Takeda**

Type 2 diabetes (Ph. III)

Aalogliptin pioglitazone **Takeda**

Type 2 diabetes (Prereg.)

Vitreosolve **Vitreoretinal Technologies**

Diabetic retinopathy (Ph. III)

Kluwer Health).

inThought Revenue forecast: \$765 million worldwide by 2017

What the analysts are saying: Contrave has a little bit more efficacy than lorcaserin (mean weight loss, 5%) but less than Qnexa (in the 8% range), and its side effect profile appears a little better than Qnexa's, although not as good as lorcaserin's. If the FDA advisory panel said lorcaserin was too weak and Qnexa was too dangerous, the obesity community is hoping Contrave is just right. We expect Orexigen to get a complete response letter but not a serious one requiring new trials.

— *Ben Weintraub, PhD, director of research, Wolters Kluwer inThought*

Oncology

PRODUCTS GENERATING BUZZ

Ipilimumab Bristol-Myers Squibb

Indication: Malignant mel. (Prereg.); prostate cancer (Phase III)
What the clinical trials found: At one year, 44-46% of melanoma patients treated with ipilimumab in a phase III trial were alive vs. 25% treated with a standard drug, and at two years, 22-24% of patients in the ipilimumab group were alive vs. 14%.
inThought Approvability Index and Comment: 61% (melanoma), 30% (prostate). The FDA told BMS it needed three more months to review ipilimumab, delaying its decision until March 26. BMS had been asked to conduct another trial, and this second phase III study lacks a control group. So BMS is going to FDA with a rather spare package, and that means there is some risk. We think it's very unlikely FDA will approve it in March, but the drug looks fairly promising, and BMS has the right trials ongoing. Having to do another study would delay approval two years. Estimated approval: January 2013 (Source: Wolters Kluwer Health).

Revenue forecast: \$1.1 billion in worldwide sales by 2015, says Tim Anderson of Bernstein Research

What the analysts are saying: Unlike PLX 4032 (see below), every patient can have this; they don't have to have any specific kind of mutation. And, really, oncologists have nothing to give these patients. What they have now is suboptimal. I don't think there will be any hesitation to put the majority of their patients on this. It will get approved and will be a high-usage product. It's also fairly easy to give, involving infusion every three weeks. — *Chantal Savelkouls, director of international projects, GfK HealthCare*

PLX 4032/RG7204 Roche/Plexxikon

Indication: Malignant melanoma (Phase III)
What the clinical trials found: This twice daily, oral small molecule selectively inhibits oncogenic BRAFV600E kinase. In a phase I clinical trial, published in *NEJM*, nearly all patients showed some response, and 81% had 30% tumor shrinkage.

inThought Approvability Index and Comment: 45%. We haven't seen a lot of data yet, but investigators have said their patients are making amazing recoveries. While this is not a peer-reviewed format that we rely on for predictive power, the buzz is very good. We will get that data next year. Estimated approval: August 2012 (Source: Wolters Kluwer Health).

What the analysts are saying: Between 50-60% of patients with melanoma have this mutation, so there will be a fairly wide-open market for PLX 4032. My guess is patients who test positive for the BRAF mutation will be put on the Roche drug first and ipilimumab (see above) second. BRAF-negative patients will be put straight on ipilimumab. The huge amount of press around this drug in the *NY Times* has boosted publicity, so physicians are very much aware of it and are very excited to be able to use it. — *Chantal Savelkouls, director of international projects, GfK HealthCare*

OTHER KEY PRODUCTS IN THE PIPELINE

Sitimagene ceradenovec Ark Therapeutics Glioma (Ph. III)

Prostate cancer vaccine (Ph. III)

Zactima (vandetanib) AstraZeneca Thyroid cancer (Prereg.)

Panobinostat Novartis Hodgkin's dis./mult. myeloma (Ph. III)

Zibotentan/ZD4054 AstraZeneca Prostate cancer (Ph. III)

Reovirus Oncolytics Biotech Head & neck cancer (Ph. III)

Regorafenib Bayer HealthCare Colorectal cancer (Ph. III)

Axitinib Pfizer RCC (Ph. III)

Talminogene laherparepvec BioVex Malignant melanoma (Ph. III)

Bosutinib Pfizer CML (Ph. III)

Tavocept (dimesna) BioNumerik Chemoprotection, lung canc. (Ph. III)

Critozinib Pfizer NSCL (Ph. III)

Brivanib (brivanib alaninate) Bristol-Myers Squibb Liver cancer (Ph. III)

Neratinib Pfizer Breast cancer (Ph. III)

Tomtovok (afatinib) Boehringer Ingelheim NSCL (Ph. III)

Tremelimumab/CP 675206 Pfizer Malignant melanoma (Ph. III)

Eribulin Eisai Breast cancer, metastatic (Prereg.)

Aplidin (plitidepsin) PharmaMar Multiple myeloma (Ph. III)

Enzastaurin Eli Lilly DLBCL, glioblastoma (Ph. III)

Afutuzumab/RG7159 Roche/Genentech NHL (Ph. III)

Tasisulam Eli Lilly Malignant melanoma (Ph. III)

Pertuzumab/RG1273 Roche/Genentech Breast cancer (Ph. III)

Genasense (oblimersen) Genta CLL (Prereg.), AML/mal. mel. (Ph. III)

Alvocidib Sanofi-Aventis CLL (Ph. III)

GSK 2118436 GlaxoSmithKline Malignant mel., NSCL (Ph. III)

Iniparib/BSI 201 Sanofi-Aventis Breast/NSCLC (Ph. III)

Ramucirumab ImClone Breast/gastric cancer (Ph. III)

Omrabulin Sanofi-Aventis Soft tissue sarcoma (Ph. III)

Custirsen Isis/Teva Prostate cancer, first/second-line (Ph. III)

Omrabulin/AVE8062 Sanofi-Aventis Soft tissue sarcoma (Ph. III)

Yondelis (trabectedin) Johnson & Johnson/PharmaMar Ovarian (Prereg.), breast/soft tissue sarc. (Ph. III)

Aflibercept Sanofi-Aventis/Bayer Colorectal/NSCL/prostate (Ph. III)

Talaporfin Light Sciences Oncology Colorectal canc. (Ph. III)

Eflornithine Sanofi-Aventis/Genzyme Familial adenomatous polyposis (Ph. III)

Ridaforolimus/MK-8669 Merck Sarcoma (Ph. III)

Brentuximab vedotin Seattle Genetics Hodgkins lymphoma (Ph. III)

DCVax-Prostate Northwest Biotherapeutics

Custirsen/TV-1011 Teva Prostate (Ph. III)

Rheumatology

PRODUCTS GENERATING BUZZ

Benlysta (belimumab) **Human Genome Sciences/GSK**

Indication: Systemic lupus erythematosus (Prereg.)

What the clinical trials found: There were two phase III trials, one showing the drug met its primary endpoint at 52 weeks, the other trending in the right direction but showing that belimumab was not quite as good at 76 weeks.

inThought Approvability Index and Comment: 62%. Although it's very exciting to have a drug nearly approved for lupus, FDA's decision and timing are not certain because the data are not perfectly clean. But we are hopeful the drug will be approved. Estimated approval: February 2011 (Source: Wolters Kluwer Health).

inThought Revenue forecast: \$1.6 billion worldwide by 2017

What the analysts are saying: HGSI shares are likely to trade higher into YE10 on one or more of the following key events: 1) a likely positive Benlysta FDA advisory panel (Nov 16th)/panel documents (Nov 12th), given the risk/reward profile of the drug in an area of significant unmet need; and 2) likely FDA approval (December 9 PDUFA date; we model for a Q1 2011 launch) and potential pricing upside.

—Salveen Richter, CFA, sr. analyst I biotechnology equity research, Collins Stewart

Tasocitinib/ CP-690,550 **Pfizer**

Indication: Rheumatoid arthritis (Phase III)

What the clinical trials found: Phase II data suggest comparability to anti-TNF therapies like Abbott's Humira. Phase III data confirm the favorable efficacy profile.

inThought Approvability Index and Comment: 62%. This oral JAK-3 inhibitor for rheumatoid arthritis (RA) would be launching into an injectable space. If you look at multiple sclerosis, people are very excited about the first FDA-approved oral drug from Novartis, Gilenya. The same thing could happen in RA (Source: Wolters Kluwer Health).

inThought Revenue forecast: \$599 million worldwide by 2016

What the analysts are saying: Tasocitinib represents a promising new mechanism of action and would be the first disease-modifying RA drug administered in pill form. While the opportunities are significant, a head-to-head trial with Humira just got under way, and physicians will want the data to determine whether tasocitinib is better or at least as good. If it is, the move to orals will be pretty quick; if it's not quite there yet, is it something physicians prescribe for earlier, less serious phases of the disease? Limited usage would limit overall market share.

—Geoff Penney, VP, category business leader, GfK HealthCare

INCB 18424 **Incyte/Novartis**

Indication: Myelofibrosis, polycythaemia vera (Phase III)

What the clinical trials found: A phase I/II trial, published in *NEJM*,

OTHER KEY PRODUCTS IN THE PIPELINE

Vimovo (naproxen/esomeprazole) **AstraZeneca**

OA, RA, ankylosing spondylitis (Ph. III)

Apremilast **Celgene**

Psoriatic arthritis (Ph. III)

Rontalizumab **Genentech**

Systemic lupus erythematosus (Ph. III)

Prochymal **Genzyme**

Crohn's disease (Ph. III)

Lodotra (Prednisone CR) **Horizon Pharma/SkyePharma**

RA (Ph. III)

INCB28050 **Incyte**

RA (Ph. II)

Xyrem (sodium oxybate) **Jazz Pharmaceuticals**

Fibromyalgia (Prereg.)

Arcoxia (etoricoxib) **Merck**

Rheumatic disorders (Ph. III)

MK-0822/Odanacatib **Merck**

Osteoporosis (Ph. III)

Naproxinod **NiCox**

Osteoarthritis (Prereg.)

AIN457 **Novartis**

Uveitis (Ph. III)

Ilaris (canakinumab) **Novartis**

Juvenile RA/idiopathic arth. (Ph. III)

PKC412 **Novartis**

Mastocytosis (Ph. III)

SMC021 **Novartis**

Osteoarthritis (Ph. III)

Aprela **Pfizer**

Postmenopausal osteoporosis (Ph. III)

Riloncept **Regeneron**

Gout (Ph. III)

R788 **Rigel**

RA (Ph. III)

REGN 88 **Sanofi-Aventis/Regeneron**

RA (Ph. III)

Laquinimod **Teva**

Crohn's disease/multiple sclerosis (Ph. III)

demonstrated marked and durable clinical benefits in patients with myelofibrosis.

inThought Approvability Index and Comment: 60%. This oral JAK2 inhibitor failed for RA but looks okay for myelofibrosis and polycythaemia vera. These are small markets, so the drug probably will not make a big impact. Some anticipate an NDA filing in late 2010 or early 2011 (Source: Wolters Kluwer Health).

What the analysts are saying: Given unmet need in polycythaemia vera (an indication larger than myelofibrosis), we estimate peak worldwide sales of ~\$750 million in FY19 in this indication alone. —Salveen Richter, CFA, sr. analyst I biotechnology equity research, Collins Stewart

Other

PRODUCTS GENERATING BUZZ

RESPIRATORY

Relovair (vilanterol + fluticasone furoate) GlaxoSmithKline/Theravance

Indication: asthma and COPD (Phase III)

What the clinical trials found: Phase II trials of this long-acting Beta 2-adrenoceptor agonist (LABA) + glucocorticoid showed evidence of 24-hour bronchodilation without the safety issues associated with salmeterol, the LABA contained in GSK's blockbuster asthma/COPD combo drug Advair. Those issues—namely an increase in asthma-related death—are contained in a black box warning on Advair.

inThought Approvability Index: 58% (Source: Wolters Kluwer Health).

What the analysts are saying: If GlaxoSmithKline can prove true 24-hour efficacy—i.e., showing that the product works over a whole day and night—and that the price is competitive, Relovair will stand a good chance on the market against twice-a-day Advair. With the threat of generic Advair receding, that's one less hurdle. Pricing could strongly impact listing on many formularies. Another potential disadvantage: vilanterol is not yet approved as a single-dose product in the US, something which could hamper physicians' comfort level with the fixed-dose combination.

—Joern Kleebach, director, GfK HealthCare

WOMEN'S HEALTH

Serada (gabapentin controlled release) DepoMed

Indication: Postherpetic neuralgia (Prereg.), hot flashes (Phase III)

What the clinical trials found: Failed to meet three out of four key goals after 12 weeks of treatment in two phase III trials, BREEZE 1 and 2. BREEZE 3 is under way.

inThought Approvability Index and Comment: 60%. An extended-release oral formulation of anti-seizure drug gabapentin, Serada helps minimize the typical side effects seen with generic gabapentin: nausea, daytime sedation and dizziness. There is a market for nonhormonal treatments for the hot flashes related to menopause. Expected approval: August 2011 (Source: Wolters Kluwer Health).

inThought Revenue forecast: \$258 million in worldwide revenue by 2018

What the analysts are saying: This is one agent we think is promising. The popular press is still weighing heavily against use of estrogen. Doctors, on the other hand, are seemingly a little more comfortable with it the last few years.

—Ben Weintraub, PhD, director of research, Wolters Kluwer inThought

OTHER KEY PRODUCTS IN THE PIPELINE

NEUROLOGY

Perampanel Eisai Epilepsy (Ph. III)

Horizant (gabapentin enacarbil) GSK Restless legs syndr. (Prereg.)

Potiga (retigabine) GSK Partial seizures (Prereg.)

Midazolam intranasal Ikano Therapeutics Seizures (Ph. III)

Bapineuzumab Johnson & Johnson Alzheimer's dis. (Ph. III)

NERI IV (edivoxetine) Eli Lilly Depression (Ph. III)

Solaneezumab Eli Lilly Alzheimer's dis. (Ph. III)

MK 4305 Merck Insomnia (Ph. III)

Telcagepant/MK-0974 Merck Migraine (Ph. III)

Sugammadex Merck Neuromuscular blockade (Prereg.)

Preladenant/SCH 420814 Merck Parkinson's dis. (Ph. III)

Vanquix (diazepam) King Epilepsy (Ph. III)

Levadox MAP Pharma Migraine (Ph. III)

Dimebon (latrepirdine) Medivation/Pfizer Alzheimer's/early stage (Ph. III)

Valdoxan (agomelatine) Novartis Depression (Ph. III)

Stedesa (eslicarbazepine) Sunovion Seizures (Ph. III)

ORPHAN DISEASE

Amigal (migalastat) Amicus Fabry's disease (Ph. III)

BiovaxID BioVest Follicular lymphoma (Ph. III)

Multikine (leukocyte interleukin) CEL-SCI Head and neck canc. (Ph. III)

Elacyt (elacytarabine) Clavis Pharma AML (Ph. III)

Calsed (amrubicin) Dainippon Sumitomo SCLC (Ph. III)

Genasense (oblimersen) Genta CLL (Prereg.), AML/mal. mel. (Ph. III)

Trizytec (liprotamase) Eli Lilly Pancreatic disorders (Prereg.)

Ceplene (histamine dihydrochloride) EpiCept AML (Prereg.)

Genz-112638 Genzyme Gaucher disease (Ph. III)

Prochymal Genzyme Graft-vs.-host disease (Ph. III)

Pasireotide/SOM230 Novartis Acromegaly/Cushing's (Ph. III)

Carfilzomib Onyx Pharma Multiple myeloma (Ph. III)

Thelein (sitaxentan) Pfizer Pulmonary hypertension (Ph. III)

Ataluren PTC Therapeutics Cystic fibrosis (Ph. III)

Firazyr (icatibant) Shire Hereditary angioedema (Prereg.)

Replagal (agalsidase alfa) Shire Fabry's disease (Prereg.)

orBec (beclometasone oral) Soligenix Graft-vs.-host disease (Ph. III)

RESPIRATORY

Injectable MPL allergy vaccine Allergy Therapeutics Seasonal allergic rhin., prevent. (Ph. III)

Azelastine/fluticasone Cipla/Meda Seasonal allergic rhinitis (Ph. III)

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

Pirfenidone InterMune Idiopathic pulmonary fibrosis (Prereg.)

SCH 697243 Merck Seasonal allergic rhinitis (Ph. III)

Ragweed allergy vaccine tablet/SCH 039641 Merck Seasonal allergic rhinitis (Ph. III)

Indacaterol Novartis COPD (Prereg.)

Indacaterol/mometasone Novartis Asthma (Ph. II)

Glycopyrrolate/indacaterol Novartis COPD (Ph. III)

WOMEN'S HEALTH

SCH 900121 Merck Contraception (Ph. III)

Elonva Merck Female infertility (Ph. III)