TRENDS-in-MEDICINE

August 7, 2011

by D. Woods
and Lynne Peterson

Quick Takes

…Highlights from this week's news relating to drugs and devices in development that are not covered in other *Trends-in-Medicine* reports…

Trends-in-Medicine
Stephen Snyder, *Publisher*
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409
Fax 772-334-0856
www.trends-in-medicine.com
TrendsInMedicine@aol.com

SHORT TAKES

- **ALLIED HEALTHCARE** – **Saga Group** is buying the company, and the deal, which must be approved by Allied's shareholders, is expected to close in 4Q11.
- **AMAG PHARMACEUTICAL** – MSMB Capital Management, a shareholder, reportedly is so disappointed in Amag's plans to buy **Allos Therapeutics** that it wants to buy AMAG and cancel the Allos deal.
- **AMYLIN and TAKEDA's premlintide/metreleptin** – The companies are discontinuing development of this combination therapy for obesity, citing "commercial" issues. An Amylin official said the company wants to develop a similar treatment with less frequent dosing.
- **APNEX MEDICAL's Hypoglossal Nerve Stimulation (HGNS) System** – The FDA said that the company can conduct a clinical study of this implantable device for obstructive sleep apnea. This alternative to standard therapy senses respiration and stimulates the hypoglossal nerve so that the tongue is forced toward the front of the mouth.
- **APOGEE's ABC-294640 and AVAXIA's AVX-470** – The Department of Health and Human Services' (HHS) Biomedical Advanced Research and Development Authority (BARDA) awarded contracts to these two companies to develop drugs to treat gastrointestinal tract injuries ≥24 hours after radiation exposure.
- **ARMGO PHARMA's s107** – A study in ***Cell Metabolism*** found that loss of muscle mass happens because of calcium seepage from the ryanodine receptor channel complex, a group of proteins found in muscle cells, suggesting that this new drug may reverse muscle loss.
- **BRISTOL-MYERS SQUIBB's subcutaneous Orencia (abatacept)** – The FDA approved this self-injectable formulation of Orencia for rheumatoid arthritis.
- **CARDIOMEMS** – The company withdrew its application to the Centers for Medicare and Medicaid Services (CMS) for a new technology add-on payment because the heart sensor device was not FDA approved for congestive heart failure (CHF) by the required July 1 deadline. The company is expected to resubmit the product later this year after it gets FDA approval. St. Jude plans to acquire CardioMEMS when the FDA approval comes through.
- **EDWARDS LIFESCIENCES' Sapien THV** – CMS reimbursement for these transcatheter aortic valve implants (TAVI) will be the same as for surgical valves, and Edwards is expected to request a new technology add-on payment once the valve has FDA approval.

- **EPIXIS' HCV vaccine** – French scientists reported in the journal ***Science Translational Medicine*** that this hepatitis C therapeutic vaccine looks promising in mouse and macaque monkey studies, even after the virus mutates, and the company hopes to start human trials in 2012. Epixis is being acquired by an undisclosed U.S. biotech company.

- **GLAXOSMITHKLINE's Avandia (rosiglitazone)** – A study to be published in the August issue of ***Anesthesia and Analgesia*** found that this controversial diabetes drug may be effective for controlling peripheral acute inflammation. A researcher said local injection of the drug produced similar effects as systemic administration in preventing the development of damage-induced neuropathic pain.

- **INSMED's Arikace** – The FDA stopped a Phase III trial of this antibiotic for nontuberculous mycobacterial lung disease and cystic fibrosis after looking at long-term data from rat studies. No humans have received doses of the drug, and the hold will be in effect until an FDA decision is made, which is expected within the next 30 days.

- **INTELLIJECT's e-cue** – The FDA tentatively approved this epinephrine auto-injector designed for use during emergency treatment of allergic reactions, dependent on the company settling a patent infringement lawsuit by **Pfizer/King Pharmaceuticals**.

- **ISTA PHARMACEUTICALS' Bromday (bromfenac ophthalmic solution)** – The FDA said the company did not submit sufficient data to prove the safety of this twice-daily eye solution if it is sold in a larger 2.4 ml size compared to the currently approved 1.7 ml bottle. The concern is that a larger fill size may increase the risk of an infection in one eye spreading to the uninfected eye.

- **MEDTRONIC's Advisa DR MRI SureScan pacing system** – The FDA gave the go-ahead for this MRI-compatible pacemaker, an advanced version of a similar cleared device, to be part of a U.S. clinical trial.

- **MERCK's ridaforolimus** – The company and its partner **Ariad Pharmaceuticals** submitted an application to the European Union for an mTor inhibitor to treat sarcoma.

- **PROTALIX BIOTHERAPEUTICS' prGCD (taliglucerase alfa)** – The company submitted its reply to the FDA's complete response letter issued in February 2011 for this plant cell-expressed recombinant glucocerebrosidase enzyme for the treatment of Gaucher disease. The application includes additional clinical data as well as the drug's chemistry, manufacturing, and controls.

- **QIAGEN's TheraScreen KRAS RGQ PCR Kit** – In July, the company submitted this companion diagnostic to the FDA with **Amgen's Vectibix** (panitumumab) in colorectal cancer. This week, in a second and separate submission, Qiagen submitted the TheraScreen as a companion diagnostic for another colorectal cancer drug, **Bristol-Myers Squibb** and **Lilly's Erbitux** (cetuximab).

- **Spinal discs** – Spinal discs made of sheep cells in a gelatinous core surrounded by a ring made of collagen were able to become one with the spine in rats, according to research published in the ***Proceedings of the National Academy of Sciences***. However, the applicability in humans is still unknown because it is not clear whether the discs will be strong enough in people.

- **SXC HEALTH SOLUTIONS** is acquiring pharmacy benefits manager PTRx and its mail-order pharmacy provider SaveDirectRx.

- **VECTURA GROUP's VR-315** – Novartis licensed rights to this generic asthma drug, which ***may*** be a generic version of **GlaxoSmithKline's Advair** (fluticasone + salmeterol), outside Europe and North America to Vectura. An undisclosed pharma licensed the U.S. rights.

- **WORLDHEART's Levacor** – The company discontinued development of this centrifugal pump left ventricular assist device (LVAD), stopping enrollment permanently in its bridge-to-transplant trial, citing delays in FDA approval of design modifications that previously had caused enrollment in the trial to be suspended. The company, which is cutting its workforce by 42%, now plans to focus on its smaller, next-generation PediaFlow and MiFlow technologies.

NEWS IN BRIEF

Acetaminophen – prescription changes advised

The National Council for Prescription Drug Programs (NCPDP), in its latest white paper, said that liver injury from acetaminophen overdose "remains a serious public health problem" and makes recommendations to provide consistency across over-the-counter (OTC) and prescription container labels. Right now, OTC containers use standardized language, but prescription drugs do not, which makes it harder for patients to know whether and how much acetaminophen is in the prescriptions they are taking. Among the NCPDP recommendations for prescription drugs are:

- Complete spelling of acetaminophen
- A standardized liver damage warning label
- Putting the warning within the top 3 warnings for a drug
- Patient education by physicians and pharmacists

ASTRAZENECA

- **Brilinta (ticagrelor).** A CRTonline.org survey asked cardiologists when Brilinta should be used: 33% said in the majority of acute coronary syndrome (ACS) patients, 30% said they need more information to decide, 27% said in clopidogrel non-responders, and 10% said in patients at high risk of stent thrombosis.
- **Caprelsa (vandetanib).** Instead of the proposed brand name Zactima, which the FDA rejected as too similar to other drugs, vandetanib will be sold as Caprelsa to treat metastatic medullary thyroid cancer. Interestingly, rather than wait for an approved brand name, AstraZeneca launched the drug, which was approved by the FDA in April 2011, under its generic name.

  The commercialization strategy was also something new for AstraZeneca. Laura Woodin, senior manager of corporate affairs at AstraZeneca, said, "It is a very different approach for us…Some companies have a dedicated rare or orphan drug division…It was a hard decision not to commercialize through our sales force at launch. Rather, we are distributing it exclusively through a specialty pharma [**Biologics**], which is a little new for us. We never did that before."

  AstraZeneca medical affairs people aren't detailing doctors on Caprelsa, but they are helping doctors understand the risk evaluation and mitigation strategy (REMS), which requires physicians to be certified in the REMS before they can prescribe the drug. Woodin said, "We don't have another drug with that level of REMS associated with it."

  However, AstraZeneca is having another problem selling Caprelsa: finding the doctors who treat medullary thyroid cancer patients. Woodin said, "Finding the doctors who specialize in this, who treat it or might see the patients, has been a challenge."
- **CPCRs.** AstraZeneca plans to collaborate with **Heptares Therapeutics** for four years to develop drugs from C-protein coupled receptors (CPCRs), with targets including inflammatory, central nervous system, and metabolic disorders.

BOEHRINGER INGELHEIM's Pradaxa (dabigatran) – more attention needed on safety issues

Two new and concerning adverse event cases were reported in the ***Archives of Internal Medicine***, both in elderly women taking it for AFib. In one case, an 88-pound, 84-year-old woman taking 75 mg BID developed massive rectal bleeding, had a cardiac arrest, and died. The other case was a 99-pound 89-year-old woman on 110 mg BID for five months who had recurrent nosebleeds and was found to have increased bleeding times and an elevated plasma level of the drug when tested prior to cochlear implant surgery. An accompanying commentary suggested that these cases should remind doctors to pay careful attention when prescribing this anticoagulant for the frail elderly and renally impaired patients.

DENDREON's Provenge (sipuleucel-T) – sales much slower than expected

The company reduced its 2011 sales projection, saying use of this prostate cancer therapeutic vaccine isn't growing as fast as expected. The company said it expects "modest" quarterly sales increases for the remainder of 2011. Dendreon blamed slow sales on physicians, saying they were not aware that CMS reimbursement is in place and were afraid of being left holding the bag for $93,000 per patient if reimbursement was denied.

EISAI's perampanel (E-2007) – filing rejected by FDA

The FDA rejected the submission for this epilepsy drug, issuing a "refusal to file" letter. The FDA wants more information on this first-in-class, highly selective, non-competitive AMPA-type glutamate receptor antagonist for the treatment of partial-onset seizures associated with epilepsy. The company said the FDA wants "reformatting and reanalyses" of some datasets but did not request new clinical or non-clinical studies.

The FDA action really is not surprising given the results of a Phase III trial reported in April 2011 at the American Academy of Neurology meeting. That trial (Study 304) in treatment-resistant epilepsy failed at both doses in the pre-specified European analysis (a 50% responder rate). In the pre-specified U.S. analysis, the 8 mg dose failed, but the 12 mg dose was statistically significant. The principal investigator, Jacqueline French, MD, of New York University (NYU), said the FDA didn't want either of these analyses, that the FDA wanted percent change in seizure frequency instead, and both doses of perampanel met the primary endpoint in that non-pre-specified analysis.

IMMUNOSYN's SF-1019 – legal problems mount

The Securities and Exchange Commission (SEC) charged four Immunosyn executives and the company's largest shareholder, **Argyll Biotechnologies**, with civil fraud, saying they lied about this drug, which is made of goat's blood and is designed to treat diseases including HIV and multiple sclerosis. Three of the executives were also charged with insider trading and securities fraud, saying the company neglected to disclose that the FDA had issued two clinical holds on new drug applications for the drug.

OUS patients in cardiac trials – might not skew the results

Research published in the ***Journal of the American College of Cardiology*** (JACC) found that international patients make up a large portion of U.S.-funded heart clinical trials, resulting in concern about whether trial results can be applied to U.S. patients. Investigators found that 19 of 24 of the trials studied included patients from countries outside the U.S. (OUS). In 11 of these, international patients made up nearly 50% of patients.

Some experts believe that results in OUS patients are not necessarily attributable to U.S. patients, but ***Reuters*** reported that Susan Shurin, MD, the acting director of the National Heart, Lung, and Blood Institute (NHLBI), disagrees, saying, "We don't see international participation in clinical trials as a negative at all."

Dr. Shurin said many of the OUS patients come from Canada, where the demographics are similar to the U.S. Even the patients from sites in Latin America and Eastern Europe (e.g., Russia and the Czech Republic) are not concerning, she said, "Our observation has been that the conduct and performance at these sites is every bit as good as it is in the U.S."

PFIZER

- **Diflucan (fluconazole) –** The FDA says that chronic, high doses (400 to 800 mg/day) of this treatment for candidiasis during the first trimester of pregnancy may be associated with a rare set of birth defects in infants. The Agency changed the pregnancy category for indications other than vaginal candidiasis from Category C to Category D, but it did not change the category for a single, low dose of the drug, which remains Category C.
- **Lipitor (atorvastatin) –** The company reportedly is considering introducing an over-the-counter (OTC) version of this cholesterol drug when it goes off patent in November 2011. *Remember that conversions to OTC can take multiple tries at the FDA, so it might not happen quickly or at all.*
- **Prevnar 13 (PCV13) –** The FDA postponed until January 2012 its decision on this pneumococcal vaccine for adults.

PTHrP – possible new treatment for osteoporosis

This natural anti-osteoporosis hormone, similar to parathyroid hormone (PTH), regrows bone quickly while preventing further bone loss in osteoporotic patients, according to a preliminary human study at the University of Pittsburgh School of Medicine that was funded by the National Institutes of Health (NIH). A researcher said, "We have made the surprising observation that continuous exposure of the human skeleton to PTH or PTHrP for one week leads to sustained but reversible suppression of bone formation. We have also provided the first evidence of a rebound increase in bone formation in human skeletons when treated with different dosing of PTH or PTHrP."

In contrast to **Lilly's Forteo** (teriparatide), a form of PTH that replaces some bone but doesn't block osteoclasts from destroying more bone, PTHrP replaces destroyed bone, replacing >5% of bone mass in just three months. Researchers hope that higher doses over a longer time can double that result. In fact, they hope to show that PTHrP is superior to PTH in a head-to-head trial.

Platelet function testing – the story may not be over

In an article in ***Cardiovascular Business News***, three platelet experts suggested trial designs that could be used to ***prove*** the

Platelet Function Testing Proposals

Measurement	Steven Manoukian, MD, Hospital Corporation of America	Matthew Price, MD, Scripps Clinic	Steven Steinhubl, MD, Geisinger Health System
Patient population	High-risk pre-PCI ACS patients with high on-treatment platelet reactivity	ACS patients undergoing PCI	All-comers for planned PCI (ACS or not)
Exclusions	Elective PCI patients; patients without high on-treatment platelet reactivity	Patients with contraindication to Lilly's Effient (prasugrel)	Recent thinopyridine, IIb/IIIa, or warfarin use
Design	High-risk hypo-responder to IIb/IIIa inhibitors vs. placebo	Prasugrel vs. platelet function-guided therapy (clopidogrel or prasugrel), using PRU >208, with individualized and non-individualized arms	Prasugrel, double-dose clopidogrel, or AstraZeneca's Brilinta (ticagrelor) non-responders randomized to either continue clopidogrel or switch to prasugrel loading dose
Endpoint	Cardiac events during and early post-procedure plus troponin-based MI	1. All-cause death, MI, or unplanned revascularization for ischemia 2. Major and minor bleeding not related to CABG 3. Net clinical outcome (composite of 1 and 2)	Cardiac events and cardiac enzymes
Size	<1,000 patients	N/A	Screen ~10,000 to enroll ~2,000
Duration	30 days, 48 hours post-PCI, or perhaps 1-year follow-up	1 year	~1 month post-PCI
Status	Trial design currently in final planning stages in U.S.	N/A	N/A

value and best use of platelet function testing, including **Accumetrics' VerifyNow**, despite the failure of the GRAVITAS trial and the early termination of the TRIGGER-PCI trial.

RECKITT BENCKISER PHARMACEUTICALS' Suboxone (buprenorphine + naloxone) and Subutex (buprenorphine) – more cost-effective than methadone

Many addiction programs, including Medicaid, limit access to buprenorphine because of concerns over cost since buprenorphine costs about $100 a month more than methadone. However, a study published in ***Health Affairs*** suggests this is incorrect thinking. The researchers found that buprenorphine is less expensive than methadone for treating substance abusers. Despite the cost of a 28% increase in relapses with buprenorphine, the drug saves ~$1,330 per year vs. methadone for maintenance treatment. And buprenorphine can be prescribed in a doctors office, while methadone is only available at special clinics.

The researchers reviewed spending, relapse events, and mortality for 33,923 Medicaid patients who were substance abusers in Massachusetts from 2003 to 2007. They found buprenorphine appeared to significantly expand access to treatment.

Suboxone recently went off patent, but no generic version is available yet. The researchers speculated that a generic Suboxone "would be likely to lower the cost of buprenorphine treatment, making the drug significantly less expensive than methadone and possibly less costly overall than drug-free treatment."

ROCHE's lebrikizumab – effective in asthma trial

Phase II study results, published in the ***New England Journal of Medicine***, for this anti-IL-13 humanized monoclonal antibody met its primary endpoint, with a statistically significant 5.5% increase in FEV_1 vs. placebo in adults with asthma whose symptoms were not controlled with inhaled corticosteroids. And patients with high levels of IL-13 had an 8.2% increase in FEV_1.

Week 12 Results with Lebrikizumab in MILLY Trial

	Lebrikizumab	Placebo
Primary endpoint: increase in pre-brochodilator FEV_1	9.8% (p=0.02)	4.3%
Any adverse events	74.5%	78.6%
Serious adverse events	3.8% (4 patients)	5.4% (2 patients)
Infections	48.1%	49.1%
Upper respiratory infections	12.3%	13.2%
Sinus infections	9.4%	8.0%
Musculoskeletal events	13.2%	5.4%

TAKEDA's Actos (pioglitazone) – new warning label

The FDA is not recalling this drug due to concerns over bladder cancer, but the Agency did update the label for this and other pioglitazone-containing medications with a new warning that the interim analysis of an epidemiologic study found this Type 2 diabetes drug may increase the risk of bladder cancer when taken for more than a year. The new label recommends against using Actos in patients with active bladder cancer and urges caution in patients with a history of bladder cancer.

TEVA and ACTIVE BIOTECH's laquinimod – fails on efficacy in Phase III trial in efficacy

This oral drug for multiple sclerosis failed to reduce relapses vs. placebo in a Phase III trial. While the drug reduced relapses by 17.6% vs. placebo, the result was not statistically significant. After adjusting for MRI differences, the drug showed a statistically significant 21% reduction in relapses, but **Biogen's Avonex** (interferon beta-1a) reduced relapses by 29% after adjustment and 26% before adjustment. Teva said it still plans to submit laquinimod to the FDA for approval.

REGULATORY NEWS

CDRH partnering with Minnesota device companies

On a trip to Minnesota to meet with device companies, Jeffrey Shuren, MD, director of the FDA's Center for Devices and Radiological Health (CDRH), announced that a new public-private partnership will be formed focusing on regulatory science, and Minnesota will be the pilot location. However, Dr. Shuren didn't provide any further details, though he suggested that computer modeling and nanotechnology could be part of it. CDRH Deputy Director of Science William Maisel, MD, said, "It's not a partnership with FDA steering the ship. Building science takes time. This is not going to be an immediate solution to problems of industry."

CMS issues new IPPS DRGs for FY2012

CMS's final rule for the FY2012 Inpatient Prospective Payment System (IPPS), which goes into effect in October 2011, doesn't appear to be as bad as some proposed rates. Hardest hit are **Allergan**'s Lap-Band, VADs, and gastric bypass. The biggest increases were for kyphoplasty/vertebroplasty, penile implant, and spinal fusion.

IPPS Changes for FY2012	
Procedure	**Change vs. FY2011**
Acute hospital inpatient (overall)	+ 1.1%
CABG	+ 1.2%
Cardiac valves	– 1.4%
DES	+ 2.2%
Gastric bypass	– 2.4%
Hip/knee replacement	0
ICDs	– 1.2%
Kyphoplasty/vertebroplasty	+ 5.9%
Lap-Band	– 5.3%
Neuromodulation	+ 1.9%
Pacemakers	+ 1.9%
Penile implants	+ 3.4%
Spinal fusion	+ 3.3%
VADs	– 2.7%

CMS reimbursement for rehab

A CMS final rule will result in a 2.2% ***increase*** in Medicare reimbursement for inpatient rehabilitation facilities (IRFs) in FY2012, 1.5% more than originally proposed in April 2011. To receive the money, IRFs will have to submit data on urinary catheter-associated urinary tract infections and pressure ulcers that are new or worsened.

CMS urged to delay e-prescribing penalties

The American Medical Association (AMA) and 91 state and specialty medical societies asked CMS to postpone the start of penalties for doctors not using e-prescribing from January 2012 to June 2012 to give doctors more time to become compliant.

Congress mulls rules for FDA advisory panels

The U.S. Congress is looking at relaxing conflict-of-interest rules set in 1970 for FDA advisory panels, which prohibit advisers from having even indirect financial ties to a deliberated product. FDA Commissioner Margaret Hamburg told a Senate Health, Education, Labor, and Pension Committee hearing that the Agency had "difficulty in recruiting highly qualified people" for panels, resulting in delays.

FDA's 510(k): small step in reform

The FDA's Dr. Maisel said the Agency will decide by the end of October 2011 whether manufacturers of medical devices that pose a ***moderate*** risk to patients should be required to provide more data to the FDA. This is just one of seven recommendations of a science panel that called for changes to the FDA's 510(k) review process.

FDA: hints about biosimilars approval process plans

When the FDA speaks, it is wise to listen, and in an article in the ***New England Journal of Medicine***, the FDA discussed its plans for implementing an approval process for biosimilars. Janet Woodcock, MD, director of FDA's Center for Drug Evaluation and Research (CDER), and other FDA officials wrote that the new approval process will be more complicated than for generic drugs, will involve analysis of much more data, and will not be a "one size fits all" approach.

The FDA expects to need to review everything from specific populations to manufacturing processes before it can decide what clinical trials will be needed for each biosimilar. However, new "fingerprint" technology that can more accurately describe a biosimilar may be helpful in making comparisons to the branded biologic. The FDA also is studying European Medicines Agency (EMA) guidelines for biosimilars, which were issued in 2005, and is expected to follow the EMA's product-specific approach.

FDA's Medical Imaging Drugs Advisory Committee

The Agency reinstated this CDER committee, effective August 5, 2011.

FDA's Office of Generic Drugs (OGD) reorganized

This division was reorganized to include another division to both the Bioequivalence and Chemistry programs and converts the Microbiology and Clinical Review staffs into divisions. It also formalizes the position of Deputy Director for Science and Chemistry. The new structure of the Office of Generic Drugs is:

- Division of Bioequivalence I
- Division of Bioequivalence II
- Division of Labeling and Program Support
- Division of Microbiology
- Division of Clinical Review
- Division of Chemistry I
- Division of Chemistry II
- Division of Chemistry III
- Division of Chemistry IV

FDA oversight of OUS ingredients

Deborah Autor, the FDA's new deputy commissioner for global regulator operations and policy, said pharmas should take more responsibility for the safety of ingredients sourced

overseas, and Congress should require pharmas to do this if they don't do so voluntarily. Autor also believes the FDA should have the power to:

- Stop drugs at the border if manufacturers refuse FDA inspections.
- Order mandatory recalls of unsafe products.

The FDA estimates that ~50% of all medical devices and 40% of drugs are made OUS, and 80% of active ingredients in U.S. drugs are manufactured OUS.

Sen. Tom Harkin, chairman of the Health, Education, Labor, and Pensions (HELP) Committee, plans to hold hearings on the global pharmaceutical supply chain this fall.

FDA to reduce device user fees

The FDA will drop user fees for medical companies by about 7% across the board in 2012.

FDA: PMA rules updated, withdrawn, and modified

The FDA announced new rules it will use to review premarket applications (PMAs) for a variety of medical devices. These standards can be used to support 510(k) applications. Among the devices affected by the changes are intraocular lenses, total hip implants, and dental implants.

OMB oversight of pharma/NIH researcher relationships questioned

The Office of Management and Budget (OMB) reportedly has proposed eliminating a publicly available website that tracks the financial relationships between pharmas and researchers who receive funding from NIH. However, Sen. Chuck Grassley (R-IA) has asked OMB to continue the online monitoring.

FDA recalls

- **AMERICAN REGENT's Vasopressin Injection**, a drug used for the prevention or treatment of postoperative abdominal distention, in abdominal roentgenography to dispel interfering gas shadows, and in diabetes insipidus – because some vials may not stay potent throughout their shelf lives.
- **ARROW's NextStep antegrade chronic hemodialysis catheters** – due to reports of breakage/separation of the stylet.
- **GE HEALTHCARE's Vital Signs Hygroscopic Condenser Humidifier (HCH)**, a passive humidification device – due to occlusions which may prevent proper flow of gases or oxygen, possibly resulting in insufficient oxygen delivered to the patient.

European approvals

- **BOEHRINGER INGELHEIM's Pradaxa (dabigatran)** – for prevention of stroke and systemic embolism in patients with atrial fibrillation. It was already approved for prevention of venous thromboembolism (VTE) in patients undergoing a hip or knee replacement.
- **MERCK's Victrelis (boceprevir)** – for the treatment of chronic hepatitis C genotype 1 infection in combination with the current standard therapy – pegylated interferon alpha plus ribavirin.

U.K.'s National Institute for Health and Clinical Excellence (NICE) actions

- **NOVARTIS' Gilenya (fingolimod)**, an oral therapy for multiple sclerosis, was determined to be too costly to be prescribed on the National Health Service (NHS).
- **THE MEDICINES COMPANY's Angiomax/Angiox (bivalirudin)** – Coverage of this direct thrombin inhibitor by the NHS was recommended in combination with aspirin and clopidogrel for STEMI patients undergoing PCI.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	August 2011	
August 12	**Physician-owned distributorships (PODs)**	Inspector General initial report due to Senate Finance Committee
August 19	FDA's draft **Strategic Plan for Regulatory Science**, including an update on the Nanotechnology Program	FDA's independent Science Board
August 20	**Regeneron's aflibercept** (VEGF Trap-Eye) for wet AMD	PDUFA date
August 25	**Shire's Firazyr** (icatibant injection) for hereditary angioedema	PDUFA date
August 30	**Seattle Genetics and Takeda's Adcetris** (brentuximab vedotin) for two orphan indications – refractory Hodgkin's lymphoma and anaplastic large cell lymphoma (ALCL)	PDUFA date
	September 2011	
September 7	Design of clinical trials for systemic antibacterial agents for the **treatment of acute otitis media**	FDA public workshop
September 8	**Johnson & Johnson's Xarelto** (rivaroxaban) for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation	FDA's Cardiovascular and Renal Drugs Advisory Committee
September 8-9	Safety of **transvaginal mesh** for pelvic organ prolapse	FDA's Obstetrics and Gynecology Devices Advisory Committee
September 9	Safety of **bisphosphonates** in osteoporosis	Joint meeting of the FDA's Reproductive Health Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee
September 13	**Anti-nerve growth factor (NGF)** drug class safety review	FDA's Arthritis Advisory Committee
September 14	**Apotex's Ferriprox** (deferiprone) for transfusional iron overload	FDA's Oncologic Drugs Advisory Committee
	Other 2011 meetings/events	
2H11	**Abbott's RX Acculink** carotid stent	FDA final decision expected
4Q11	**Ophthotech's ARC-1905** primary endpoint results in Phase I trial in dry AMD	Company announcement or medical conference presentation
4Q11	**Roche/Genentech's Lucentis** (ranibizumab) – Phase III HARBOR trial one-year data on the 2 mg dose in wet AMD	Company announcement or medical conference presentation
October 17	**Teva Neuroscience's Azilect** (rasagiline mesylate) for a new indication in Parkinson's disease	FDA's Peripheral and Central Nervous System Drugs Advisory Committee
October 28	**Bristol-Myers Squibb and AstraZeneca's dapagliflozin,** the first SGLT-2 for Type 2 diabetes	PDUFA date
October 28	**Pacira Pharmaceuticals' Exparel** (bupivacaine extended-release liposome injection), a painkiller	PDUFA date
December	**Allergan's brimonidine tartrate intravitreal implant** – Phase II trial in dry AMD to complete	Company announcement or medical conference presentation
December 8	**Antares Pharma's Anturol** (transdermal oxybutynin ATD gel), a treatment for overactive bladder	PDUFA date
December 13	**Endo Pharmaceuticals' Opana** (extended-release oxymorphone), a painkiller	PDUFA date
	2012 meetings/events	
January	**Pfizer's Prevnar 13** (PCV13), a pneumococcal vaccine for adults	PDUFA date
February	**Alcon's tandospirone** for dry AMD – Phase III final data expected	Company announcement or medical conference presentation
February 17	**Corcept Therapeutics' Corlux** (mifepristone) for Cushing's syndrome	PDUFA date
February 28	**Pfizer's axitinib** for advanced renal cell carcinoma	PDUFA date (*approximate*)
April 30	**Vivus' avanafil** for erectile dysfunction	PDUFA date (*approximate*)
April 30	**Baxter and Halozyme's HyQ** for immunodeficiency	PDUFA date