TRENDS-in-MEDICINE

March 4, 2012

by 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
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SHORT TAKES

- **ATRICURE's AtriClip –** The FDA gave the company permission to test this left atrial appendage closure device as a stand-alone procedure in up to 30 patients. The trial will start in 2H12.
- **AVI BIOPHARMA's AVI-7288 –** The company was given permission to continue testing this drug to treat Marburg virus infection.
- **BAVARIAN NORDIC's Imvanexr**, a smallpox vaccine, was submitted to the European Medicines Agency for approval. It is also awaiting approval in Canada.
- **BRISTOL-MYERS SQUIBB's Eliquis (apixaban) –** The PDUFA date for this anti-coagulant was extended to June 28, 2012, because new information the company provided to the FDA constituted a major amendment and reset the review clock. *We first warned in mid-February that this delay was likely. We also believe there may be an advisory committee review on May 23, but that is not official yet.*
- **COLUMBIA LABORATORIES and WATSON PHARMACEUTICALS' Prochieve (progesterone gel 8%) –** The FDA followed the advice of its Reproductive Health Drugs Advisory Committee and rejected this vaginal gel for pre-term birth prevention for lack of efficacy, issuing a complete response letter that said additional studies will be required for approval. As a result, Columbia cut its workforce by 42% to save money.
- **DBV TECHNOLOGIES' Viaskin Peanut**, an epicutaneous immunotherapy, was granted fast track status by the FDA to desensitize patients with a peanut allergy.
- **ENDO PHARMACEUTICALS** will ask shareholders in May 2012 to approve a change in the company's name to **Endo Health Solutions**.
- **Eye drops –** The FDA's Dermatologic and Ophthalmic Drugs Advisory Committee, concerned about cross-contamination, voted 10-1 against *labeling* that would allow a single bottle of anti-inflammatory eye drops to be used for two individual eyes post-operatively.
- **Flu vaccine –** A study of 13 million older Canadians over nine flu seasons, published in the ***Archives of Internal Medicine***, found that vaccination was associated with reductions in hospitalization for pneumonia and influenza as well as a small decrease in all-cause mortality during the flu season but not at other times of the year.
- **GALAPAGOS' GLPG-0634 – Abbott Laboratories** agreed to pay $150 million for the initial rights to this JAK1 inhibitor for rheumatoid arthritis (RA).

- **GLOBUS MEDICAL's NuBone** – The company reached a settlement with the FDA that resolves the FDA's complaint that Globus was marketing an unapproved medical device – NuBone, an allograft tissue product derived from cortical bone – that the FDA had declined to approve. Under the settlement, Globus agreed to pay a $550,000 penalty, and the company's CEO agreed to pay an additional $450,000 penalty.

- **JOHNSON & JOHNSON's Xarelto (rivaroxaban)** – The FDA granted priority review for a new indication for this anticoagulant – to treat acute coronary syndrome (ACS).

- **OCTAPHARMA's Octaplas LG** – The company submitted a biological license application (BLA) to the FDA for this treatment for managing preoperative or bleeding patients who require replacement of multiple plasma coagulation factors. The company also is seeking approval for use as a substitute for intentionally removed plasma, such as plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP).

- **SCIENCE APPLICATIONS INTERNATIONAL** received a $78 million contract from the Centers for Medicare and Medicaid Services (CMS) to help reduce potential fraud in a cloud services model by providing identity-proofing and credentialing information technology (IT) services.

- **Smoking cessation** – A 12-week, 479-patient study published in the ***European Respiratory Journal*** found that nicotine replacement therapy mouth spray is twice as effective in helping smokers quit as patches and gums. The study found that 14% of smokers who used the mouth spray for three months did not smoke at one year vs. 6% of placebo smokers.

- **Technetium-99** – Canadian scientists suggested that hospitals with cyclotrons may be able to make their own technetium-99, which is in very short supply, by modifying machines used to make other isotopes. They said the retrofit is relatively simple and can produce commercial quantities of this radiopharmaceutical at a reasonable cost. The problem is whether the technetium-99 produced by the cyclotrons would meet medical safety standards and whether the production process would meet nuclear safety guidelines.

- **TRISTAR HEALTH SYSTEM** has formed a "clinical affiliation" with **MinuteClinic**, a division of **CVS Caremark**. TriStar physicians will act as medical directors for the retail clinics in CVS stores in the Nashville area, will collaborate on patient education and disease-management initiatives, and will work toward integrating their electronic health-records (EHRs).

- **ULTRAGENYX PHARMACEUTICAL's UX-003**, a therapeutic compound for Sly syndrome, was granted orphan drug status by the FDA.

NEWS IN BRIEF

Antiepileptic drugs – medical societies urge report withdrawal

Four medical societies – the American Academy of Neurology (AAN), the American Epilepsy Society, the International League Against Epilepsy, and the Epilepsy Foundation – joined together to urge the U.S. Agency for Healthcare Research and Quality (AHRQ) to withdraw its report on antiepileptic drugs, which compared the efficacy, safety, and tolerability of newer vs. older and brand vs. generic antiepileptic medications, saying the report fails to take into account the complexities of epilepsy and the drugs used to treat it.

BIOGEN IDEC

- **Avonex (interferon-beta-1a).** The prescribing information for this multiple sclerosis drug was updated to include an optional titration regimen at the start of therapy designed to reduce flu-like symptoms: gradual dose escalation over four weeks, starting with 7.5 µg and increasing in 7.5 µg increments weekly up to the regular dose of 30 µg.

- **BG-12 (dimethyl fumarate).** The drug was submitted to the FDA as an oral BID therapy for multiple sclerosis.

BOEHRINGER INGELHEIM's Pradaxa (dabigatran) – more concern raised about bleeds

In a letter published in the ***New England Journal of Medicine***, New Zealand hematologists called for better prescriber education because of concern about a "cluster" of bleeding episodes in patients treated with the anticoagulant. The doctors said many of the bleeds were in older patients and renally-impaired patients, with prescriber errors in ~25% of the complications, which they said suggested a lack of awareness of the potential risks associated with the drug.

The Hematology Society of Australia and New Zealand formed a panel to investigate bleeding, and their two-month audit of medical records found 78 bleeding incidents, including 12 major bleeds, one of which might have contributed to the patient's death. They also identified several factors associated with bleeding complications: prescriber error, renal impairment, age >80, body weight <60 kg, and lack of reversibility.

CARDINAL HEALTH loses Round 2 – judge allows DEA to stop Florida opioid shipments

U.S. District Judge Reggie Walton ruled in favor of the Drug Enforcement Administration, saying Cardinal Health must stop shipping drugs from its Lakeland FL distribution center. The judge had issued a temporary restraining order preventing the DEA from enforcing its February 2, 2012, suspension of Cardinal's license to distribute controlled substances from the distribution center. However, Cardinal may transfer its controlled substance inventory from the Lakeland facility to other Cardinal distribution centers.

Justice Department lawyer Clifford Lee Reeves said companies like Cardinal have a responsibility to ensure that the products they ship are not being abused, and the judge agreed, saying companies "have an obligation…to self-police in order to track unusually large drug shipments that may signal diversion beyond their proper use." Cardinal said it plans to ship the controlled substances from other facilities.

CELGENE's Thalomid (thalidomide) – effective in cutaneous lupus

A 60-patient study published in the ***British Journal of Dermatology*** found that low-dose thalidomide successfully induced complete response in a majority of patients with refractory cutaneous lupus erythematosus. The patients were given 100 mg of Thalomid daily and followed for 8 years, with 98% achieving a clinical response and 85% having a complete response. Patients with subacute cutaneous lupus were 30 times more likely to achieve long-term remission after treatment discontinuation while those with discoid lupus were significantly more likely to relapse with treatment discontinuation.

Ebola – possible treatment discovered

Laboratory experiments described in the journal ***Science Translational Medicine*** suggested that **Novartis' Gleevec** (imatinib) and **Tasigna** (nilotinib) may be an effective therapy for Ebola. In cell culture studies, both drugs stopped the release of viral particles from infected cells by blocking c-Abl1, a tyrosine kinase protein that Ebola requires to replicate.

ENDO PHARMACEUTICALS' Symmetrel (amantadine hydrochloride) – early improvement in TBI

A randomized, multicenter study by Harvard researchers, published in the ***New England Journal of Medicine***, found that patients with severe traumatic brain injury (TBI) recovered function more rapidly when treated with Symmetrel than placebo. And the improvements were in clinically meaningful behaviors, such as consistent responses to commands, intelligible speech, reliable yes-or-no communication, and functional-object use.

Once treatment was stopped, the placebo-treated patients had more rapid improvement vs. the amantadine patients, and both groups had similar improvements by the end of the study. However, the researchers concluded, "In view of the health-care cost constraints and declining lengths of stay for inpatient rehabilitation, amantadine-induced acceleration of recovery may represent an important advance."

GEDEON RICHTER and FOREST LABORATORIES' cariprazine (RGH-188) – positive Phase III data

The companies said this antipsychotic met the primary endpoint in two Phase III trials in schizophrenia, and they plan to submit it this year to treat schizophrenia and bipolar mania.

- In a 617-patient fixed-dose trial vs. **Bristol-Myers Squibb's Abilify** (aripiprazole) vs. placebo, cariprazine decreased symptoms (hallucinations, emotional withdrawal, guilt, and anxiety) 6 points with 3 mg and 8.8 points with 6 mg.
- In a 446-patient flexible dosing study, 3-6 mg cariprazine reduced symptoms 6.8 points, and 6-9 mg reduced symptoms 9.9 points.

Industry guidelines – updated rules on giveaways

The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) issued updated guidelines for interactions between doctors and industry. Among the requirements in the updated Code of Practice:

- Member companies must train all employees about the difference between gifts and promotional aids vs. items of medical utility.
- Permitted items include:
  - incidental refreshments and/or meals with background music at meetings or other events (but not the funding of a concert, tickets to events, etc.) or similar entertainment, or offering tickets to events.
  - Low-value, low-volume items such as pens or notepads but not electronics or gift baskets.
  - Personal gifts in special situations.
  - Infrequent distribution of items of medical utility (e.g., anatomical models and medical textbooks).
  - Funding to patient organizations if the company is not the sole funding source.

Omega-3 fatty acids – needed for brain functioning

A study published in ***Neurology*** found that low levels of omega-3 fatty acids can cause memory problems by causing the brain to age faster and lose some of its thinking abilities. In the 1,575-patient study sponsored by the National Heart, Lung, and Blood Institute and the National Institute on Aging, people whose docosahexaenoic acid (DHA) levels were in the lowest quartile had lower brain volume on magnetic resonance imaging (MRI) scans and scored lower on visual memory and executive function tests vs. people with higher DHA levels.

ROCHE's Rituxan (rituximab) – may treat cryoglobulinemic vasculitis

Two studies published in ***Arthritis & Rheumatism*** found that this B-cell inhibitor effectively alleviates serious manifestations of cryoglobulinemic vasculitis, a systemic vasculitis. In a 24-patient study, 83% of Rituxan patients were in remission at 6 months vs. 8% of those on conventional therapy. In a 59-patient trial, 64.3% of Rituxan patients were on therapy at one year vs. 3.5% of those on standard therapy. Both studies were terminated early because of the high response rate with Rituxan.

Sleeping pills – increase mortality and perhaps cancer

Even short-term use of sleeping pills – e.g., **Sanofi's Ambien** (zolpidem), **Novartis' Restoril** (temazepam), **Dainippon Sumitomo Pharma/Sepracor's Lunesta** (eszopiclone], and **Pfizer's Sonata** (zaleplon) – more than triples the mortality risk vs. non-users, according to a study published in ***BMJ Open***. Researchers from the Scripps Clinic Vierbi Family Sleep Center in La Jolla CA and the Jackson Hole Center for Preventive Medicine reviewed electronic medical records (EMRs) and identified >10,000 patients using sleeping pills, comparing them to a matched cohort of nearly 24,000 non-users. They found a 3.6 times increased risk of death in patients who used 1-18 pills in any given year vs. non-users.

Over 2.5 years, the risk of death was 4.43 times for patients prescribed 18 to 132 pills and 5.32 times greater among those prescribed more than 132 doses vs. non-users. Overall mortality was 1.2% for non-users vs. 6.1% for sleeping pill users. The study also found an increase in cancer cases among sleeping pill users.

Statins – FDA issues new warnings

The FDA issued several new warnings about statins – lovastatin, **Merck's Zocor** (simvastatin), **Pfizer's Lipitor** (atorvastatin), **AstraZeneca's Crestor** (rosuvastatin), and others. The FDA is not questioning the benefit of statins [for] lowering cholesterol. The label changes include:

- Removing the need for routine periodic monitoring of liver enzymes.
- New information about memory loss and confusion.
- Warnings about the potential risk of increased blood sugar levels and of being diagnosed with Type 2 diabetes.
- New information about drug interactions with protease inhibitors used to treat HCV or HIV.

Stroke – role of antibodies investigated

A study in ***Archives of Neurology*** found that patients with acute stroke were more likely than those with other conditions to have antibodies in their cerebrospinal fluid (24.8% vs. 2.5%, $p<0.001$). The German researchers said, "The strong association between cerebrospinal fluid-specific immunoglobulin synthesis and stroke suggests a role in the development of cerebral ischemia and might constitute an immunologically defined stroke subgroup."

Diagnostic tests are not routinely performed on cerebrospinal fluid in patients after an ischemic stroke, and the researchers called for a "systematic prospective analysis of cerebrospinal fluid and serum samples to determine the time kinetics and pathogenicity of antibodies." The researchers studied data from 3,050 consecutive patients with an ischemic stroke. Only 10.4% (318) had a lumbar puncture within 96 hours of symptom onset. Those 31 were compared to 79 controls who did not have a stroke but did have a lumbar puncture.

TAKEDA's TAK-875 – positive Phase II data in Type 2 diabetes

A 12-week, 426-patient study published in ***The Lancet*** found that this investigational diabetes drug lowered HbA_{1c} as much as glimepiride (48% vs. 40%) but with fewer adverse events in Type 2 diabetics, including less hypoglycemia. Mean HbA_{1c} at Week 12 was down 1.12% with TAK-875 50 mg/day vs. -1.05% with glimepiride and -0.13% with placebo. Hypoglycemia occurred in 2% of TAK-875 patients vs. 19% of glimepiride patients ($p=0.01$). Adverse events occurred in 49% of TAK-875 patients vs. 61% of glimepiride patients. A Phase III trial is under way.

REGULATORY NEWS

CMS pays less than private payors for TKR

A study by the non-profit Health Care Incentives Institute found that Medicare pays 14% less (-$6,400) for total knee replacements (TKRs) than private payors. The study reviewed data on 19,000 Medicare surgeries and 32,000 commercial procedures, and found the average cost for the 180 days surrounding the surgery was $22,611 for Medicare patients and $25,872 for private payors. *Will this spur private payors to bundle payments as a way to lower reimbursement?*

CMS test for the need for CT scans not reliable

A study published in the ***Annals of Emergency Medicine*** found that the measure CMS developed to determine whether brain CT scans are necessary for emergency department patients who present with non-trauma-related head pain – the Outpatient Measure 15 (OP-15) – is not reliable and should be eliminated. Researchers found the CMS measure had an overall accuracy of only ~17%. One of the problems is the OP-15 often doesn't take into account the patient's other symptoms or history.

Some states denying Medicaid coverage for ED visits

The American College of Emergency Physicians (ACEP) reported that Medicaid officials in some states are denying coverage of emergency room treatment based on the final diagnosis codes rather than the symptoms that brought the patient to the emergency department (ED). ACEP said Medicaid officials are increasingly implementing plans to deny payment for ED services if the patient is ultimately determined to have a non-urgent condition.

For example, patients who present to the ED with chest pains would be covered by Medicaid in all states if it turns out to be a myocardial infarction, but if the final diagnosis is heartburn, then some states are denying payment even though the hospital and doctor can't know it is heartburn until a heart attack and other conditions are ruled out. The concern is that Medicare and other payors might follow suit and attempt to deny coverage based on final diagnosis.

Senate rejects contraception coverage exemption

The Senate voted 51-48 against an amendment by Sen. Roy Blunt (R-MO) that would have allowed insurers to deny coverage of health services – e.g., birth control – if an employer objected on religious or moral grounds.

FDA approvals/clearances

- **ABBOTT's Absolute Pro** stent was granted expanded premarket approval for use in treating patients with narrowed iliac arteries. It was already approved as a biliary stent.
- **APTALIS**
  - **Ultresa (pancrelipase)**, a delayed-release capsule, was approved to aid digestion in cystic fibrosis patients.
  - **Viokace (pancrelipase)** was approved for use with a proton pump inhibitor to aid digestion in adults with pancreatitis or who underwent surgery to remove the pancreas.
- **ASTRAZENECA's FluMist Quadrivalent** – This vaccine that protects against four strains of flu (two strains of A and two strains of B) was approved for people ages 2 to 49.
- **BIOGEN IDEC's pen-type intramuscular injector** was approved to allow multiple sclerosis patients to self-inject Avonex (interferon beta-1a).
- **CAS MEDICAL SYSTEMS' Fore-Sight Oximeter** was cleared by the FDA for determining whether newborns are at risk for low oxygen saturation levels, which are linked to serious damage to multiple organs.
- **MERIDIAN BIOSCIENCE's TRU Legionella**, a test to spot bacteria linked to Legionnaires' disease, was cleared for use.
- **OTSUKA AMERICA PHARMACEUTICAL's BreathTek UBT test** received expanded approval for use in children ages 3-17 to detect the *Helicobacter pylori* bacterium, which can cause ulcers, gastritis, and certain cancers.
- **TEVA's Pharmachemie BV unit** was approved to sell preservative-free methotrexate to treat cancer.
- **VARIAN MEDICAL SYSTEMS' Surface Beacon Transponder** for the Calypso System received 510(k) clearance for use to monitor motion during radiotherapy.

FDA recalls/warnings

- **Automated external defibrillators (AEDs)** – **Cardiac Science's Powerheart**, **CardioVive**, and **CardioLife**; the **GE Responder** and **Responder Pro**; and **Nihon-Kohden** AEDs were all recalled for a defective component.
- **FRESENIUS'** subsidiary **APP Pharmaceuticals** received a warning letter about generic drugs produced at its plant in Grand Island NY.
- **GLAXOSMITHKLINE's DynaCirc (isradipine CR)** – The company recalled nearly 400,000 bottles of this antihypertensive because of "inconsistent" packaging at the **Novartis** plant where it was made.

- **GLENMARK GENERICS' norgestimate/ethinyl estradiol** – Seven lots of this oral contraceptive were recalled because some pills were packaged out of sequence.
- **MERCK's Januvia (sitagliptin)** – The FDA issued a warning letter because Merck failed to conduct the required 3-month postmarket rodent study of the risk of pancreatitis by the June 15, 2011, deadline. Merck's initial design for the study was rejected by the FDA as inadequate, and the company never submitted a revised protocol. Instead, Merck submitted data from an investigator-initiated study in mice, but the FDA said that did not meet the requirements. Now, Merck says it will submit a final protocol for the safety study within 30 days and will begin the study in six months. *But the FDA is not happy. The Agency has become much less tolerant of companies dragging their feet on postmarket requirements.*
- **PFIZER's Prevnar 13 pneumococcal vaccine** – One lot was recalled because it contained "expired" material.
- **THORATEC's HeartMate II**, a left ventricular assist device (LVAD) – Thoratec received a warning letter from the FDA that:
  - It did not report a patient death to the FDA in a timely manner (even though it was allowed to report in 90 days rather than the usual 30 days).
  - It did not report malfunctions in a timely manner.
  - It is not conforming with cGMP quality standards.

European regulatory actions

- **British regulators** now recommend annual examinations for anyone who has a metal-on-metal hip implant to ensure they are not experiencing soft-tissue damage or other problems as long as they have the implant, not just for five years, as they initially recommended.
- **GEDEON RICHTER/PREGLEM's Esmya (ulipristal)** was approved for pre-operative treatment of uterine fibroids.
- **KONING's Koning Breast CT,** a 3D system for early detection of breast cancer, was granted a CE Mark.
- **NOVARTIS' Glivec (imatinib, Gleevec in the U.S.)** – The European Commission updated the label for this drug to allow use up to 36 months as adjuvant therapy for KIT-positive gastrointestinal stromal tumors (GIST) if the estimated recurrence risk is >50%.
- **TAKEDA and AFFYMAX's peginesatide** – The EMA accepted the marketing application for this anemia therapy for dialysis patients.

Canadian regulatory news

- **BIOPTIGEN's Envisu**, a hand-held eye-scanning device, was approved. It also has a CE Mark and is awaiting FDA clearance.
- **PURDUE PHARMA's OxyContin and OcyNEO** – Several Canadian provinces, including Ontario, have stopped subsidizing these painkillers in an effort to fight opioid abuse.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	March 2012	
March 6	**Discovery Labs' Surfaxin** (lucinactant) for infant respiratory disease	PDUFA date
March 6	**Eisai and Astex Pharmaceuticals' Dacogen** (decitabine) to treat acute myeloid leukemia (AML) in older patients	PDUFA date
March 7	**NeurogesX's Qutenza** (transdermal capsaicin) for neuropathic pain	PDUFA date
March 7	Design and methodology for **postmarketing studies**	FDA Public Workshop
March 12	Safety of **anti-nerve growth factor (anti-NGF) drugs** in development to treat a variety of pain conditions. The questions are: Do reports of joint destruction represent a safety signal, and does the risk:benefit balance favor continued development?	FDA's Arthritis Advisory Committee
March 13	**Discussion of appropriate target populations**, objectives, and designs of trials to evaluate drugs to treat hyperbilirubinemia in newborns. In the afternoon, a discussion of development of an unnamed investigational drug	FDA's Gastrointestinal Drugs Advisory Committee
March 20	**GlaxoSmithKline's Votrient** (pazopanib) for advanced soft-tissue sarcoma (in the morning), and **Merck/Ariad's Taltorvic** (ridaforolimus) for maintenance therapy of metastatic soft-tissue sarcoma or bone sarcoma (in the afternoon)	FDA's Oncologic Drugs Advisory Committee (ODAC)
March 21	**Talon Therapeutics' Marqibo** (vincristine sulfate liposomes injection) for Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL)	FDA's Oncologic Drugs Advisory Committee (ODAC)
March 22-23	Consideration of **broadening the eligibility for changing prescription drugs to over-the-counter medications**	FDA public meeting
March 23	Risk:benefit of **Stryker's Wingspan**, a self-expanding nitinol stent already in use under an HDE for treatment of intracranial arterial stenosis	FDA's Neurological Devices Advisory Committee
March 26	**MAP Pharmaceuticals' Levadex** (dihydroergotamine inhalation) for migraine	PDUFA date
March 26-27-28	Oral arguments on the **legality of Obamacare**	U.S. Supreme Court
March 27	**Affymax and Takeda's peginesatide** for anemia	PDUFA date
March 27	**Shire's Replagal** (agalsidase alfa) to treat Fabry disease	FDA's Cardiovascular and Renal Drugs Advisory Committee
March 28	**Chelsea Therapeutics' Northera** (droxidopa) for symptomatic neurogenic orthostatic hypotension with primary autonomic failure	PDUFA date
March 28	**Edwards Lifesciences' Sapien** transcatheter aortic valve	CMS expected to publish National Coverage Decision (NCD) memo
March 28-29	Two-day discussion of pre-and post-approval assessment of **cardiovascular safety for diet drugs and biologics**	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
	April 2012	
April 2	Types of consumer studies needed to assess proper use of a **MedKit containing doxycycline** in the event of **anthrax exposure**	FDA's Anti-Infective Drugs Advisory Committee meeting jointly with the Non-Prescription Drugs Advisory Committee
April 5	**Astellas' Betanis** (mirabegron), a beta-3-adrenoceptor agonist to treat overactive bladder (OAB)	FDA's Reproductive Health Drugs Advisory Committee
April 11	**U-Systems' Automated Breast Ultrasound (ABUS) scanning device** for breast cancer detection in asymptomatic dense-breasted women	FDA's Radiological Devices Advisory Committee
April 12	Possible reclassification of **breast transilluminators**, which are currently pre-amendment Class III devices, and **blood irradiators**	FDA's Radiological Devices Advisory Committee
April 17	**Vivus' Qnexa** (phentermine + topiramate) for weight loss	PDUFA date for resubmission
April 25	**Takeda's alogliptin**, a DPP-4 for Type 2 diabetes	PDUFA date
April 25	**HeartWare's HVAD** left ventricular assist device	FDA's Circulatory System Devices Advisory Committee
April 26	**Amgen's Xgeva** (denosumab) for prevention/delay of bone metastases in castration-resistant prostate cancer	PDUFA date
April 26	Topic **TBA**	FDA's Circulatory System Devices Advisory Committee
April 27	**Salix Pharmaceuticals and Progenics Pharmaceuticals' Relistor** (methylnaltrexone injection) for opioid-induced constipation	PDUFA date
April 29	**Vivus' avanafil** for erectile dysfunction	PDUFA date
April 30	**Baxter and Halozyme's HyQ** for immunodeficiency	PDUFA date

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	Other 2012	
2Q12	**Arena Pharmaceutical and Eisai's Lorqess** (lorcaserin) for weight loss	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
May 1	**Protalix Biotherapeutics' taliglucerase alfa**, an investigational Gaucher disease drug	PDUFA date
May 4	**Alexza Pharmaceuticals' Adasuve** (loxapine inhalation powder) for the acute treatment of agitation associated with schizophrenia/bipolar I disorder	PDUFA date
May 10 or 11 (?)	**Gilead Sciences' Truvada** (emtricitabine + tenofovir) for HIV prevention	FDA's Antiviral Drugs Advisory Committee
May 13	**Talon Therapeutics' Marqibo** (vincristine sulfate liposomes injection) for Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL)	PDUFA date
May 23 **(?)**	**Bristol-Myers Squibb's Eliquis** (apixaban), an anticoagulant for prevention of stroke in AFib	FDA's Cardiovascular and Renal Drugs Advisory Committee (*this is not official yet but expected*)
May 30-31	Discussion of **analgesic treatment of chronic pain** – mechanisms, epidemiology, new data on opioid efficacy, etc.	FDA Public Workshop
June	**Forest Laboratories and Ironwood Pharmaceuticals' linaclotide** for IBS-C	PDUFA date
June 5	**Salix Pharmaceuticals' crofelemer** for HIV-related diarrhea	PDUFA date
June 8	**Roche/Genentech's pertuzumab** in HER2+ advanced breast cancer	PDUFA date
June 15	**Gilead Sciences' Truvada** (emtricitabine + tenofovir) for HIV prevention	PDUFA date
June 25	**QRxPharma's MoxDuo** (morphine + oxycodone)	PDUFA date
June 26	**Edwards Lifesciences' Sapien** transcatheter aortic valve	CMS final NCD expected
June 28	**Bristol-Myers Squibb's Eliquis** (apixaban), an anticoagulant for the prevention of stroke in AFib	***New*** PDUFA date
June 29	**Astellas Pharma's mirabegron** for treatment of overactive bladder	PDUFA date
July 26	**Amarin's AMR-101** (omega-3 fish oil EPA) to treat hypertriglyceridemia	PDUFA date
July 26	**Horizon Pharma's Lodotra** (low-dose prednisone) for rheumatoid arthritis	PDUFA date
July 27	**Onyx Pharmaceuticals' carfilzomib** for multiple myeloma	PDUFA date
July 30	**Regeneron's Arcalyst** (rilonacept) for gout	PDUFA date
August 21	**Pfizer's tofacitinib**, an oral JAK2 inhibitor for rheumatoid arthritis	PDUFA date
August 27	**Gilead Sciences' Quad** (emtricitabine + tenofovir + elvitegravir + cobicistat) for HIV	PDUFA date
October 21	**Impax Laboratories' IPX-066** for Parkinson's disease	PDUFA date