TRENDS-in-MEDICINE

February 19, 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
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

- **Antihypertensives** – A study published in the ***American Journal of Hypertension*** found that, of 52,039 patients who received a new prescription for an antihypertensive between 1994 and 2002, 50% were not taking their medication a year later and 19.4% stopped after the first prescription.
- **APOTHÉCURE**, a Dallas-based mail order compounding pharmacy, was charged with two misdemeanor criminal violations of the Federal Food, Drug, and Cosmetic Act because of a February 2007 shipment of a gout drug containing some vials with dosages more than seven times stronger than what was shown on the label, and some with strengths about two-thirds those shown, that was blamed for three deaths.
- **BIOGEN** is buying **Stromedix**, which develops therapies for fibrosis and organ failure, including STX-100, which is starting a Phase II trial in idiopathic pulmonary fibrosis.
- **BOSTON SCIENTIFIC's Synergy** – Preliminary data from a randomized trial published in the ***Journal of the American College of Cardiology*** showed this everolimus-eluting stent with a bioabsorbable polymer coating was non-inferior to the company's Promus Element, a drug-eluting stent with a durable polymer coating, in patients with symptomatic coronary artery disease (CAD). Synergy also was non-inferior in terms of in-stent late loss at 6 months (the primary angiographic endpoint).
- **CSL BEHRING** – The company's recombinant fusion protein linking coagulation Factor VIIa with albumin, a potential therapy to treat hemophilia, was granted orphan drug status by the FDA.
- **GE** and **Microsoft's** new joint venture in healthcare technology will be called **Caradigm**. The companies plan to combine some of their existing health IT products and develop a new technology platform and clinical applications for Caradigm.
- **IPSEN's taspoglutide** – A 24-week, randomized, double-blind, placebo-controlled study published in the journal ***Diabetes Care*** found that weekly taspoglutide injections were associated with improved glycemic control and reduced body weight in Type 2 diabetics. HbA_{1c} was reduced much more with taspoglutide 10 mg and 20 mg in patients with a baseline >8.0% than in patients with a baseline <8.0%.
- **JOHNSON & JOHNSON's canagliflozin** – A randomized, double-blind, placebo-controlled, parallel-group, 28-day, 29-patient study published in the journal ***Diabetes, Obesity and Metabolism*** found that this SGLT-2 inhibitor benefited Type 2 diabetics with poor glycemic control with insulin therapy.

- **LUMERIS** is buying an ownership stake in **NaviNet**, which claims to be the largest real-time communications network for physicians and hospitals in the U.S. NaviNet tracks administrative, financial, and clinical transactions by physicians, and Lumeris offers technological tools and management systems for doctors and hospitals to monitor costs and quality of care.

- **NOVARTIS' Menveo (quadrivalent meningococcal vaccine)** – The FDA rejected approval of this vaccine for infants and toddlers (age 2 months to 2 years), issuing a complete response letter asking for more data. The vaccine already is approved for ages 2-55.

- **REGENERON's Eylea (aflibercept)** – At least one case of sterile intraocular inflammation has been associated with this anti-VEGF drug for age-related macular degeneration. The expected rate is 0.05%, and the Eylea rate may be within that since the company said it has only had reports from one site. *This bears watching.*

- **SANOFI's semuloparin** – The SAVE-ONCO study results, published in the ***New England Journal of Medicine***, found that this ultra-low-weight molecular heparin, a blood thinner, reduced the risk of blood clots in patients undergoing certain cancer treatments. The event rate fell from 3.4% with placebo to 1.2% with semuloparin.

- **TETRAPHASE PHARMACEUTICALS' TP-434** – The company received a government contract from the Biomedical Advanced Research and Development Authority (BARDA) worth up to $67 million to develop this investigational antibiotic as a potential countermeasure against bioterrorism – as a treatment for inhalational diseases caused by harmful pathogens such as *Bacillus anthracis*, *Francisella tularensis*, and *Yersinia pestis*. TP-434 is also being developed to treat serious hospital infections.

NEWS IN BRIEF

ACTELION

- **Clazosentan.** Rat data from Wayne State University – to be presented at the American Academy of Neurology meeting in April 2012 – found that this edothelin receptor A (EtrA) inhibitor may shield against the harmful effects of traumatic brain injury (TBI) by blocking the receptors that contribute to the restriction of blood flow after TBI. The preliminary data showed that clazosentan decreased reduction in blood flow by 25% at 4 hours and by 23% at 48 hours post-TBI, but the results were mixed at 12 hours. Clazosentan was most effective when given at 2 hours post-injury and then again at 24 hours post-injury.

- **Macitentan.** The company said it still hasn't figured out why 120 patients out of 740 died in a Phase III trial of this dual endothelin receptor antagonist in pulmonary arterial hypertension (PAH). In September 2011, the drug failed in a Phase II trial in idiopathic pulmonary fibrosis (IPF). Actelion is continuing development in PAH, and the Phase III SERAPHIN trial is fully enrolled, with results expected in 1H12.

ASTELLAS PHARMA's gamma-secretase modulators – beat gamma-secretase inhibitors

A report in the ***Journal of Neuroscience*** by Astellas researchers said that γ-secretase inhibitors do nothing to improve memory in mice with Alzheimer's disease when given subchronically and can even worsen the condition in normal mice. On the other hand, a γ-secretase modulator sharpened memory in transgenic mice.

BRACCO DIAGNOSTICS' CardioGen-82 – coming back on market

The FDA notified the medical imaging community that this positron emission tomography (PET) scanner that uses strontium to evaluate the heart is coming back on the market, but with a boxed warning, revised labeling, and enhanced testing information. The company voluntarily recalled the scanner in July 2011 over concerns about patients being exposed to excessive radiation. However, that was later found to be operator error, not product malfunction.

The revised labeling establishes new "Alert Limits" for strontium-82 (Sr-82) and strontium-85 (Sr-85) levels in the generator eluate. Clinical sites are also advised to "strictly follow" the new directions for use and to review and update the instructions for their dose calibrators to ensure proper isotope readings are performed in the eluate testing procedures.

Gene therapy – promise in preventing epileptic seizures

A study by University of Florida researchers that was published in the journal ***Neuroscience Letters*** found that gene therapy could be used to stimulate production of somatostatin – a seizure-stopping neuropeptide in the brain – and thus perhaps prevent seizures in epileptics. People with epilepsy (or Alzheimer's disease) tend to have lower levels of somatostatin.

Boosting somatostatin levels led to weaker and shorter seizures, and none of the patients with temporal lobe epilepsy

who received the gene therapy injections suffered the highest level of seizure. Furthermore, the treatment did not result in unwanted side effects. This is early research, and many questions still need to be answered, including: how best to deliver it in humans (injection to the brain or IV infusion) and where in the brain to deliver it.

Ghrelin – possible treatment for cancer-related appetite loss

A small (41-patient) study, funded by the Japanese government and published in the journal ***Cancer***, found that a synthetic version of this "hunger hormone" might help limit the loss of appetite often associated with cancer chemotherapy. The researchers gave ghrelin infusion to patients undergoing cisplatin treatment for advanced esophageal cancer vs. a saline control. The ghrelin patients maintained better appetites and were able to take in almost 50% more calories per day than patients given saline. Ghrelin patients also had much less nausea and anorexia than saline patients.

GILEAD SCIENCES

- **GS-7977.** In the ongoing ELECTRON trial, a two-drug regimen of GS-7977 + ribavirin failed to suppress the hepatitis C virus in genotype 1 (HCV-1) patients who were prior null responders to pegylated interferon + ribavirin. The company said six of the eight evaluable prior null responders relapsed within four weeks after completing the 12-week regimen.
- **Truvada (emtricitabine + tenofovir).** The FDA granted priority review to the supplemental NDA (for a new indication) for this HIV drug – to prevent HIV infection. An FDA advisory panel is scheduled for sometime in May 2012, and the PDUFA date is June 15, 2012. The AIDS Healthcare Foundation has come out against approval, saying that a 44% efficacy rate in preventing HIV infection is not sufficient.

Healthcare IT – EHR adoption growing

The number of hospitals using healthcare information technology (HIT) more than doubled from 2009 to 2011. According to a survey conducted by the American Hospital Association, 35% of hospitals had EHRs in 2011 vs. 16% in 2009. Furthermore, 85% of hospitals now expect to take advantage of Medicare incentive payments by 2015.

In addition, Health and Human Services Secretary Kathleen Sebelius announced that nearly 2,000 hospitals and more than 41,000 doctors received a total of $3.12 billion in incentive payments for achieving "meaningful use" of HIT, particularly electronic health records (EHRs). In January 2012, CMS paid $519 million to eligible providers.

Hypothermia – may reduce mortality in sepsis patients

A study published in the American Thoracic Society's ***American Journal of Respiratory and Critical Care Medicine*** found that external cooling of septic shock patients for 48 hours made shock reversal significantly more common vs. uncooled patients and reduced 14-day mortality. However, there was no significant difference in mortality at ICU discharge or at hospital discharge, so the researchers said they could not make definitive conclusions on the mortality effect, and larger studies are needed.

LMWH – beats warfarin in preventing cancer-related blood clots

A study reported in ***The Oncologist*** found that low-molecular-weight heparin (LMWH) may be better than warfarin for preventing recurrent blood clots in cancer patients. This is in line with American Society of Clinical Oncology (ASCO) guidelines, which recommend the use of LMWH for clots linked to cancer.

Methylphenidate – mixed results on cardiac risk

A study published in the ***American Journal of Psychiatry*** found that adults taking this attention-deficit/hyperactivity disorder (ADHD) medication may be at increased risk for adverse cardiovascular events, but the drug may not be causal. The researchers found, after examining a cohort of nearly 220,000 patients, that new methylphenidate users had almost twice the risk for sudden death or ventricular arrhythmia than age-matched controls, but the drug dose "was inversely associated with risk."

MICROCHIPS – positive early results on drug-delivery technology

Researchers at MIT, Massachusetts General Hospital, and Harvard Medical School used a MicroCHIPS chip to automatically deliver generic teriparatide (**Lilly's Forteo**) to seven women with osteoporosis. The tiny drug-delivery microchip, which can be inserted in a doctor's office, delivered a pre-programmed dose, and that dose could be changed externally, like a pacemaker can be reprogrammed, using a radio signal. The test chip contained 20 doses of the drug, sealed in tiny reservoirs. Blood tests done at 12 months found the rate of

bone formation was similar to when the women self-injected the drug.

Omega-3 fatty acids
– may help in retinitis pigmentosa

A retrospective analysis of three clinical trials published in the ***Archives of Ophthalmology*** found that a combination of vitamin A supplementation and a diet high in omega-3 fatty acids may slow the loss of visual acuity for patients with retinitis pigmentosa. Previously, the researchers from the Massachusetts Eye and Ear Infirmary reported that a high intake of omega-3 fatty acids + vitamin A helps preserve central visual field sensitivity. Thus, they concluded that a regimen of vitamin A + an omega-3-rich diet "should make it possible for many patients with typical retinitis pigmentosa to retain both visual acuity and central visual field for most of their lives."

PFIZER

- **Chantix (varenicline).** A small, non-randomized, pilot study published in ***Alcoholism: Clinical and Experimental Research*** found that 15 heavy social drinkers/light smokers who took this smoking cessation drug experienced increased dysphoria after consuming alcohol and a reduction in their ratings of liking alcohol.
- **Tafamidis meglumine** was granted priority review by the FDA to treat transthyretin familial amyloid polyneuropathy, a rare neurodegenerative disorder. It is already approved in Europe and sold as **Vyndaqel**.

TAKEDA's Velcade (bortezomib)
– effective in amyloidosis

Two studies published in ***Blood***, the journal of the American Society of Hematology, reported preliminary success in treating AL amyloidosis with a combination of Velcade, cyclophosphamide, and dexamethasone (CVD) – a combination commonly used to treat multiple myeloma. The studies concluded that this combination therapy can produce a complete hematologic response in some patients and may allow them to become eligible for stem cell transplants:

- A 17-patient study found the combination produces rapid and complete hematologic responses in the majority of patients, regardless of previous treatment or stem cell transplant candidacy, and may also help non-eligible patients to become eligible for stem cell transplant.
- A 43-patient retrospective study found the combination effective and leading to high hematologic responses. In addition, rapid improvement in organ function was observed.

TNF inhibitors
– may not increase cancer risk in JIA after all

New research reported in the journal ***Arthritis & Rheumatism*** found that the cancer rate in children with juvenile idiopathic arthritis (JIA) is four times higher than in normal children, but the study also found that treatments including tumor necrosis factor (TNF) inhibitors – e.g., **Amgen's Enbrel** (etanercept), **Abbott's Humira** (adalimumab), and **Johnson & Johnson's Remicade** (infiximab) – which have a boxed warning in their labels about a possible cancer risk, may not be to blame.

Using Medicaid database records, the researchers identified 7,812 children with JIA and two comparator groups without JIA. They found that the incidence of cancer was 4.4 times higher for probable and highly probable malignancies in JIA patients, and pediatric JIA patients treated with methotrexate without a TNF inhibitor had a similarly increased risk (3.9 times higher than non-JIA children).

In an accompanying editorial, University of Chicago researchers cautioned that larger studies with longer follow-up are needed to confirm these findings, but they noted that the underlying cancer risk associated with JIA may have been understated, "The greater frequency of malignancy does not appear to be necessarily associated with treatment, including use of TNF inhibitors."

UNITEDHEALTH/OPTUM
– launches healthcare data cloud

UnitedHealth Group's Optum health-services unit is starting a healthcare-focused cloud-computing platform for providers and insurers. The company will allow third-party developers to offer apps to users. Optum reportedly hopes to be the Apple of healthcare, getting healthcare data out of hospitals, doctors' offices, and insurance claims departments and moving it to a secure cloud-based environment. Optum's partners in the effort include Cisco, EMC, Hewlett-Packard, and IBM.

REGULATORY NEWS

CMS extended timeline on ICD-10 implementation

ICD-10 was scheduled to be mandatory as of October 1, 2013, but the Centers for Medicare and Medicaid Services (CMS) has postponed that, saying that the Department of Health and Human Services (HHS) will announce a new compliance date in the future. The announcement was not unexpected since just a few days before this, Marilyn Tavenner, RN, acting administrator of CMS, told the American Medical Association

Advocacy Conference that CMS planned to re-examine the ICD-10 timeframe. She indicated that providers and hospitals may have more on their plates than they can handle, given the demands of meaningful use and the creation of healthcare information exchanges (HIEs), "We're trying to listen to that and be responsive."

CMS proposed new rules on overpayments

CMS proposed that providers and suppliers must report and return self-identified overpayments either within 60 days of the incorrect payment being identified or on the date when the corresponding cost report is due – whichever is later. This is the newest step in CMS' efforts to prevent overpayments from occurring in the first place.

The Affordable Care Act gave CMS the ability to set an explicit deadline for provider repayment of overpayments. Overpayments include: Duplicate submission of the same service or claim, payment to the incorrect payee, payment for excluded or medically unnecessary services, or payment for non-covered services. A failure to report and return the overpayment within the timeframe could be considered a violation of the False Claims Act, which carries severe penalties.

DEA still trying to shut down Cardinal distribution center in Florida

A hearing was held on Monday, February 13, 2012, in Washington DC on efforts by the Drug Enforcement Administration (DEA) to block distribution of opioids by not only two Florida **CVS** pharmacies but also from the Cardinal distribution center that serves them. The federal judge presiding in the matter ordered the DEA to explain within a week its rationale for issuing warrants to shut down the distribution center. The judge said he wants to make sure the DEA is not shutting down a business without due process, and he said he can't determine that from simply reviewing the suspension order without more information from DEA. *So, the saga isn't over. Stay tuned.*

FDA budget proposal

President Obama's proposed FY2013 budget holds the FDA budget allocation from Congress relatively flat at $2.5 billion. This means that additional funds for the Agency have to come from user fees, and the budget proposes seven new user fees in addition to reauthorizing prescription drug and medical device fees that are set to expire at the end of September 2012. It also increases existing fees.

Some of the features in the proposed FDA budget are:

- $10 million to expand inspections in China. This includes $4.4 million for food inspection and $5.6 million for drug plant inspections. The FDA has had an office in China since 2009.
- User fee increases of $643 million over the previous year, with $364 million of this coming from generic drugs and biosimilar products and $253 million from food producers.
- $156 billion in pharma discounts over the next 10 years for drugs sold to low-income seniors.
- A $63 billion in cuts over the next 10 years to post-acute care hospitals and nursing homes.
- Cuts in imaging by raising the assumed use rate for advanced imaging devices and implementing a prior-authorization program in Medicare for advanced diagnostic imaging.

FDA issues heparin production guidance

The FDA issued draft guidance designed to ensure the safe production of the blood-clot prevention drug heparin, but it comes four years after the active ingredient in **Baxter International's** heparin was found to have been contaminated in China with oversulfated chondroitin sulfate (OSCS), causing deaths, a congressional investigation, and a huge furor. The guidance document said the contaminant appears to have been intentional adulteration to reduce the cost of production, but it was Chinese suppliers, not Baxter, who were implicated in the contamination.

Baxter sold its heparin business last year to **Hikma Pharmaceuticals**, and Hikma claims to use only U.S.- or Canada-sourced materials to make heparin for the U.S. market.

The FDA now recommends testing for the species of origin and the presence of OSCS in each shipment of crude heparin before manufacturing. The FDA also said heparin manufacturers should audit their suppliers. The guidance will be open for public comment for 60 days.

FDA warnings found to fall short

A report published in the journal ***Medical Care*** charged that many FDA drug-risk communications may have a delayed effect, unintended consequences, or no effect at all on drug monitoring or prescribing behavior. The researchers analyzed data from 49 studies covering 16 drugs or therapeutic classes and found that inappropriate co-prescribing seemed to decrease over time, but clinical practice often took months to years to respond to the warnings. In addition, advisories sent out more than once appeared to have more effect in decreasing new medication use than they did in reducing overall use.

HIV/AIDS funding gets a budget boost

President Obama's FY2013 budget calls for an ~10% increase in HIV funding for the Ryan White AIDS Drug Assistance Program (ADAP), up $102 million from the FY2012 level of $1 billion. Other HIV-related budget news included:

- A $20 million increase in the fund for primary care of HIV/AIDS patients.
- An $8 million decrease in HIV programs for children, youths, women, and families.
- No change in the NIH research budget for HIV.
- No change in funding for the CDC's Hepatitis Prevention program (~$30 million).

The National Alliance of State and Territorial AIDS Directors (NASTAD) estimates that there are currently 4,118 people on ADAP waiting lists in 12 states and >445 people in six states who have been removed from the program due to budget constraints and growing enrollment. Each year >32,500 people enroll in ADAP.

Bill speeds drugs for serious/life-threatening diseases

Senator Kay Hagan (D-NC) introduced a bill, titled "Transforming the Regulatory Environment to Accelerate Access to Treatments (TREAT) Act," to get targeted treatments to patients with serious or life-threatening diseases approved faster by the FDA. She compared this approach to that used to advance HIV and cancer drugs back in the 1990s.

The TREAT Act would accelerate the review and approval process for medicines that treat an unmet medical need, that significantly advance the standard of care, or that are highly targeted therapies for serious or life-threatening diseases or conditions.

The bill is being referred to the Senate Health, Education, Labor, and Pensions Committee, which oversees healthcare issues.

10-month SGR fix

The House of Representatives voted 293-132 to pass a compromise bill that delays for 10 months the pending 27% cut in Medicare physician pay rates that was due to go into effect. The Senate also approved the bill by a vote of 60-36 less than an hour later. *Well, well, another relatively short-term fix instead of a solution, so doctors have to go through this again at the end of the year!*

FDA approvals/clearances

- **BIOSANTE and TEVA's Bio-T-Gel (transdermal testosterone)** was approved to treat men with hypogonadism. Teva will handle marketing.
- **CORCEPT THERAPEUTICS' Korlym (mifepristone)** was approved to treat patients with endogenous Cushing's syndrome who have Type 2 diabetes or glucose intolerance and are not candidates for surgery or who have not responded to prior surgery. Korlym should never be used (contraindicated) by pregnant women without a Risk Evaluation and Mitigation Strategy (REMS). Korlym will be distributed through a central pharmacy, not retail pharmacies.
- **ELEKTA's Integrity R1.1**, a digital control system for the company's linear accelerators, received 510(k) clearance.
- **GEN-PROBE's Progensa PCA3**, a molecular assay to help evaluate whether men who previously had negative prostate biopsies need to undergo a repeat biopsy, was cleared for use.
- **HOSPIRA's** manufacturing plant in Rocky Mount NC was given permission by the FDA to resume production of injectable drugs while it resolves quality control issues.
- **KONICA MINOLTA's Aero DR** wireless system, a flat-panel detector, was cleared for use.
- **MEDASYS' Prometra**, an implantable, programmable pump for intraspinal administration of Infumorph (preservative-free morphine sulfate sterile solution), received PMA approval.
- **MEDICREA's PASS MIS** surgical device was cleared.
- **MEDTRONIC's Resolute**, a next-generation zotarolimus-eluting stent, was approved.
- **MERCK's Zioptan (tafluprost)**, a prostaglandin analog eye drop for open-angle glaucoma, was approved.
- **NLT SPINE's Prow Fusion**, a product for minimally-invasive spine surgery, received 510(k) clearance.
- **SIEMENS' Biograph mCT PET/CT scanner** – The FDA approved several features incorporated into this scanner, including the OptisoHD detector system; features that correct images and adjust for user variation; and applications that capture quantifiable measurements in cardiology, oncology, and neurology imaging.
- **SUSPENSION ORTHOPAEDIC SOLUTIONS' Distal Clavicle Fracture Fixation System** and the **Mid-Shaft Clavicle Plate**, for shoulder repairs, both received 510(k) clearance.

FDA recalls/warnings

- **ACCURATE SET** was barred by the FDA from making and selling a variety of dental products due to violations at its manufacturing facility. The FDA obtained a court order requiring the company to discontinue operations until the FDA has verified its dental implants meet federal standards.
- **FLIGHT MEDICAL INNOVATIONS** updated its voluntary recall of remote alarm cable, part number V24-00400-29, used to connect a Newport HT50 mechanical ventilator to a nurse station.
- **Hand-held dental x-ray units** – The FDA warned dentists that these devices that have not been reviewed by the FDA are illegal and potentially unsafe but are being sold by manufacturers outside the U.S. who ship them to buyers in this country.
- **INTEGRA LIFESCIENCES** – The FDA sent the company a warning letter, citing ongoing problems with mold at its collagen manufacturing facility in Plainsboro NJ.
- **JOHNSON & JOHNSON/MCNEIL's Tylenol** – Another recall! This time seven lots (~574,000 bottles) of infant grape-flavored Tylenol oral suspension due to consumer complaints about difficulty using the SimpleMeasure dosing system, which includes a dosing syringe.
- **MERCK KGAA** – The FDA sent the company a warning letter, saying that three of its plants (two in Switzerland and one in Italy) are not in compliance with cGMP, citing numerous violations.
- **ROCHE/GENENTECH's Avastin (bevacizumab)** – The FDA sent letters to 19 medical practices in California, Texas, and Illinois, warning them that they may have purchased a counterfeit version of Avastin 400mg/16mL from **Quality Specialty Products** (also known as **Montana Health Care Solutions** and distributed by Volunteer Distribution), which even might have been used. The counterfeit version is labeled as Avastin but does not contain bevacizumab. Roche conducted laboratory tests that confirmed the vials are counterfeit and said the vials might have the Roche label instead of a Genentech label. The FBI is investigating.
- **SANOFI/GENZYME's Fludara (fludarabine)** – The company recalled one batch (9,380 vials) of this leukemia drug due to a "lack of assurance sterility." The drug was manufactured at **Boehringer Ingelheim's** Ben Venue Laboratories.

European regulatory actions

- **BEN VENUE LABORATORIES.** The European Medicines Agency (EMA) said that its final recommendation is that prescriptions can resume for 12 drugs manufactured at the company's Ohio plant: Angiox (bivalirudin), Busilvex (busulfan), Vidaza (azacitidine), Vistide (cidofovir), Velcade (bortezomib), Ecalta (anidulafungin), Soliris (eculizumab), Cayston (aztreonam), Luminity (perflutren), Mepact (mifamurtide), Torisel (temsirolimus), and Vibativ (telavancin).
- **CARTIHEAL's Agili-C**, a cartilage defect repair product, received a CE Mark based solely on a preclinical study.
- **EDWARDS LIFESCIENCES' Intuity** – This aortic valve made of bovine pericardial tissue was granted a CE Mark.
- **European Medicines Agency** issued a guideline for drugmakers on how to take patients' genetic variability into consideration when assessing how the body reacts to drugs. The guideline on pharmacogenetic methodology in pharmacokinetic evaluation of treatments will apply to all companies applying for marketing approval beginning August 1, 2012.
- **GLAXOSMITHKLINE's Tyverb (lapatinib, Tykerb in the U.S.)** – GSK withdrew its EMA application to expand use of this breast cancer drug after regulators said the lack of an active controlled trial would make it difficult for them to make a decision.
- **MERCK's Victrelis (boceprevir)** – The EMA recommended updated prescribing information for this hepatitis C virus (HCV) drug because of interactions with HIV protease inhibitors atazanavir (Bristol-Myers Squibb's Reyataz), darunavir (Johnson & Johnson/Tibotec's Prezista), and lopinavir (Abbott's Kaletra).
- **Orlistat** – Roche's Xenical and GlaxoSmithKline's Alli – The EMA said the benefits of these diet drugs outweigh the risks in patients with a body mass index ≥28 kg/m^2, but the EMA recommended the labels discuss the liver damage risk.

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

ROCHE's Tarceva (erlotinib) – NICE said it wants more information before approving this for first-line treatment of non-small-cell lung cancer (NSCLC). NICE requested a cost-effectiveness analysis vs. **AstraZeneca's Iressa** (gefitinib).

Regulatory actions in other countries

MEDIPOST's Cartistem – Korea's Food and Drug Administration approved commercial sales of this stem cell therapy derived from newborn umbilical cord blood and injected into a patient's knees to help regenerate cartilage. Final U.S. clinical trials are expected to start in 2015.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	February 2012	
February 22	**Vivus' Qnexa** (phentermine + topiramate), a diet drug	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
February 23	**Chelsea Therapeutics' Northera** (droxidopa) for symptomatic neurogenic orthostatic hypotension with primary autonomic failure	FDA's Cardiovascular and Renal Drugs Advisory Committee
February 23	**Forest Laboratories' Eklira** (aclidinium bromide) for chronic obstructive pulmonary disease (COPD)	FDA's Pulmonary-Allergy Drugs Advisory Committee
February 27	The portion of the meeting on appropriate types of evidence for approval of anti-inflammatory drugs for post-op inflammation and pain in patients ***was canceled***, but Topic 2, the portion of the meeting on the appropriateness of marketing a single bottle of **anti-inflammatory ophthalmic products for use in both eyes for post-surgical indications, will still take place as scheduled**, as it relates to the potential risk for infection.	FDA's Dermatologic and Ophthalmic Drugs Advisory Committee
February 28-29	Flu vaccine update, including **Pandemic Influenza Surveillance** and licensure pathways for pandemic flu vaccines	FDA's Vaccines and Related Biological Products Advisory Committee
	March 2012	
March 3	CMS National Coverage Decision on **TAVR** ends	CMS public comment period ends
March 6	**Discovery Labs' Surfaxin** (lucinactant) for infant respiratory disease	PDUFA date
March 6	**Eisai's 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 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 28	**Bristol-Myers Squibb's Eliquis** (apixaban) to prevent strokes in AFib	PDUFA date – delayed but new date not available. FDA panel is May 23.
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 NCD decision 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

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	April 2012	
April 5	**Astellas' mirabegron**, a beta-3-adrenoceptor agonist to treat overactive bladder (OAB)	FDA's Reproductive Health Drugs 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
2Q12	**Arena Pharmaceutical and Eisai's Lorqess** (lorcaserin) for weight loss	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
	Other 2012	
May TBA	**Gilead Sciences' Truvada** (emtricitabine + tenofovir) for HIV prevention	FDA's Antiviral 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 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
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 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