TRENDS-in-MEDICINE

February 5, 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…

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SHORT TAKES

- **Advertising** – According to a Nielsen report, pharma spending to advertise their drugs decreased 23% from 2007 to 2011, and the trend is expected to continue.
- **ARENA PHARMACEUTICAL and EISAI's Lorqess (lorcaserin)** – The company said it expects the FDA's Endocrinologic and Metabolic Drugs Advisory Committee to review Lorqess in 2Q12.
- **BARCO**, a healthcare imaging company, is acquiring **JAOtech**, a manufacturer of patient entertainment and point-of-care terminals for hospitals.
- **BTG's Varisolve (polidocanol endovenous microfoam)** – The company said that a 590-patient, Phase III VANISH-2 trial met the efficacy endpoints with no significant safety concerns. This is the first of two Phase III U.S. trials of this injectable varicose vein therapy.
- **CELL THERAPEUTICS' Pixuvri (pixantrone)** – The company pulled its resubmitted new drug application (NDA) for this non-Hodgkin's lymphoma (NHL) drug after the FDA refused to delay the date of the advisory panel. The company had requested more time to prepare for the Oncologic Drugs Advisory Committee meeting, which had been scheduled for February 9, 2012. The company plans to submit it again later this year.
- **DIAMYD THERAPEUTICS' GAD-alum** – In a study published in the ***New England Journal of Medicine***, GAD-alum failed to reduce C-peptide levels, improve glucose, or reduce the need for insulin in Type 1 diabetics. The researchers are hopeful that they may still find a subset of patients who may benefit.
- **e-prescribing** – A study at two Australian hospitals, published in ***PLoS Medicine***, found that the use of electronic prescribing systems resulted in statistically significant reductions in medication errors, though the effect was limited by system-related mistakes. The researchers said the clinical error rate increased from 1.02 to 1.39 errors per admission with implementation of e-prescribing, but after adjusting for system-related errors, the rate dropped to 0.83 with e-prescribing.
- **IMPAX LABORATORIES** licensed **AstraZeneca's Zomig** (zolmitriptan), a migraine drug, getting the non-exclusive rights to develop new products containing Zomig and to exclusively commercialize them under the Zomig brand name in the U.S.
- **INFINITY PHARMACEUTICALS' saridegib** – The company halted a 122-patient Phase II trial in pancreatic cancer of chemotherapy ± saridegib after a preliminary analysis found that patients receiving chemo alone survived longer than those with saridegib added.

- **iROBOT** is investing in **InTouch Health**, a telemedicine company with which it had previously partnered to develop healthcare applications on iRobot platforms. The new arrangement allows iRobot access to FDA-regulated health-care facilities, including hospitals, operating rooms, etc.

- **Ketamine –** Researchers are conducting a test of a single infusion of this glutamate antagonist anesthetic – which is used illegally as "Special K" – as a rapid treatment for severe depression. If that test is successful, they plan a second study of three-times-a-week dosing to test the drug's long-term effects.

- **LILLY's solanezumab –** The company said an independent safety monitoring committee cleared its two 18-month Phase III trials of this Alzheimer's drug (which clears amyloid beta in the brain) to continue. Data are expected in mid-2012 from both trials.

- **MERCK's Gardasil (human papillomavirus quadrivalent) –** A Merck-sponsored study of the health records of ~190,000 California females aged 9-26 concluded that this human papillomavirus (HPV) vaccine does not trigger autoimmune disorders such as rheumatoid arthritis, lupus, Type 1 diabetes, Graves' disease, optic neuritis, or multiple sclerosis (MS). The 2-year study was published in the ***Journal of Internal Medicine***.

- **MESOBLAST –** The FDA gave the company permission to begin a 3-month Phase II trial of its off-the-shelf injectable stem cell therapy for Type 2 diabetes.

- **NOVARTIS' Focalin (dexmethylphenidate) –** The FDA's Pediatric Advisory Committee recommended that this attention-deficit/hyperactivity disorder (ADHD) drug have a boxed warning in the label about the risk of suicidal thoughts in children. FDA reviewers cited eight cases of suicidal ideation over the past six years and urged that the label warn about angioedema and anaphylaxis as well. The Focalin label already contains a warning about new psychotic or manic symptoms but does not mention suicidal ideation. The only other ADHD drug with suicidal ideation mentioned in the label is **Lilly's Strattera** (atomoxetine), which includes that warning in a black box.

- **Pancreatic enzymes –** The FDA's Pediatric Advisory Committee recommended that three forms of pancrelipase – **Abbott's Creon** (pancrelipase protease), **Aptalis' Zenpep** (pancrelipase lipase), and **Johnson & Johnson's Pancreaze** (pancrelipase amylase) – no longer need special monitoring for viral transmission related to the porcine nature of the product and can go back to routine monitoring during abbreviated reviews.

- **SPECTRUM PHARMACEUTICALS' Zevalin (Yttrium-90 ibritumomab tiuxetan) –** A study published in ***Cancer*** suggested that patients with relapsed or refractory lymphoma who are being prepared for autologous stem cell transplant (ASCT) may do better if Zevalin is added to high-dose chemotherapy before the transplant.

- **STEMCELLS' HuCNS-SC –** The company got approval from the FDA to begin a human trial of this stem cell therapy for dry age-related macular degeneration.

- **SUCAMPO and TAKEDA's lubiprostone** met the primary endpoint in a 439-patient Phase III trial in the U.S. and Europe in opioid-induced bowel dysfunction. The company plans to submit a supplemental NDA to the FDA in 1H12.

- **TEVA's Plan B One-Step (levonorgestrel) –** The FDA's Pediatric Advisory Committee recommended that this morning-after emergency contraceptive be returned to routine monitoring after the FDA said it had received no reports of fatalities between 2002 and 2010.

- **ZIOPHARM ONCOLOGY's Zymafos (palifosfamide) –** The company said the independent data monitoring committee recommended continuation (without changes) of the Phase III PICASSO-3 in metastatic soft tissue sarcoma.

NEWS IN BRIEF

Diabetes drugs – linked to pancreatic cancer

A study published in the ***American Journal of Gastroenterology*** found that common diabetes drugs – metformin, sulfonylurea, and insulin – may be linked to an increased risk of pancreatic cancer. Using data from the U.K.'s General Practice Research Database, the researchers identified 2,763 patients with newly diagnosed pancreatic cancer between 1995 and 2009 as well as 16,578 matched controls. They found that short-term use of metformin, sulfonylureas, and/or insulin had no real impact on the risk of pancreatic cancer, but long-term use of any of these drugs appeared to significantly increase the risk.

EDWARDS LIFESCIENCES' Sapien – new data somewhat lessen safety concerns with TA

The transapical (TA) continued access protocol (CAP) data from Cohort A of the PARTNER Trial were presented at the Society of Thoracic Surgeons (STS) meeting, and the data showed that mortality and stroke remain a problem with the TA approach to transcatheter aortic valve replacement in elderly patients, but they aren't quite as big an issue as they

initially appeared to be. With >800 Sapien patients in the CAP analysis:

- Thirty-day mortality was 8.2% (vs. 8.7% in earlier data), and 1-year mortality was 23.6% (vs. 29.1% in earlier data).
- The 1-year stroke rate was 3.7% in CAP, down from 10.8% in PARTNER TA patients.

Watch for the TA CAP details in a major medical journal.

Heart failure – novel approach generating interest

A small study published in the ***Journal of the American College of Cardiology*** described a novel approach to improving endothelial function in heart failure – ursodeoxycholic acid (UDCA), a bile acid commonly used in the treatment of cholestatic liver disease. In the prospective, double-blind, crossover, 17-patient European study, the 500 mg BID for 4 weeks significantly improved peak post-ischemic blood flow in the arm (p=0.038) and showed a trend for improvement in peak post-ischemic blood flow in the leg (p=0.079), but it failed to show any benefit in exercise capacity or inflammatory markers. European Society of Cardiology (ESC) experts said the data, though mixed, warrant investigation in a larger study.

Kenneth Dickstein, MD, PhD, a cardiologist from Norway and an ESC spokesperson, said, "Although the study failed on two out of three counts, the observed improvements in post-ischemic arm and leg blood flow make it highly unlikely such findings would have occurred purely by chance. The results are enough to pique real interest and suggest the approach has the potential to offer another string to our bow for improving heart failure symptoms."

The theory behind UDCA is that abdominal congestion caused by heart failure leads to increased gut permeability, allowing endotoxins produced by gram-negative bacteria to enter the circulation. Increased levels of proinflammatory cytokines then further exacerbate symptoms of heart failure. UDCA forms a complex ("mixed micelles") around a component of the cell wall of the gram-negative bacteria (lipopolysaccharide), decreasing levels of proinflammatory cytokines and potentially improving peripheral blood flow and increasing exercise tolerance.

PFIZER

- **Chantix (varenicline).** In a small (37-patient) study published in the journal ***Drug and Alcohol Dependence***, this smoking cessation drug failed to significantly reduce cocaine dependence (the primary endpoint), but researchers said there was a trend to lower odds of cocaine use that suggests it may have utility in treating cocaine dependence.
- **Prevnar 13 pneumonia vaccine.** The FDA's Pediatric Advisory Committee agreed that the estimates of febrile seizure risk with this vaccine need to be further refined and that routine monitoring of the vaccine should continue.
- **Xalkori (crizotinib).** Researchers at Massachusetts General Hospital found another subtype of non-small cell lung cancer (NSCLC) – ROS1+ – where this drug is effective in addition to the ALK+ cancers. ROS1-driven tumors account for 1%-2% of NSCLC. The findings were published in the ***Journal of Clinical Oncology***. Patients with ROS1+ tumors tend to be younger, never-smokers with adenocarcinoma, a profile similar to that of ALK+ patients. There is a diagnostic test to identify ROS1+ tumors.

Proton pump inhibitors (PPIs) – increased risk of hip fracture in postmenopausal women

A study funded by the National Institutes of Health and published in ***BMJ*** found that postmenopausal women who use PPIs regularly have an increased risk of hip fracture, particularly if they have ever smoked. For women who used PPIs for two years, there was a 35% increased risk vs. women who never used PPIs. The fracture risk increased by more than 50% in current smokers.

Among the nearly 80,000 women in the study, almost 900 hip fractures occurred in the 8-year period studied. That translates to ~2.02 fractures for every 1,000 person-years for PPI users vs. 1.51 fractures per 1,000 person-years for non-users. The researchers suggested that inhibition of calcium absorption from smoking may act synergistically with PPIs to increase fracture risk.

Psoriasis – new guidelines allow first-line biologics use

New psoriasis treatment guidelines from the National Psoriasis Foundation, published in the ***Archives of Dermatology***, say that newer biologic agents – e.g., **Amgen's Enbrel** (etanercept), **Abbott's Humira** (adalimumab), and **Johnson & Johnson's Remicade** (infliximab) – can be considered for first-line use in moderate-to-severe plaque psoriasis because they do not carry the risk of end-organ toxicities found with older, conventional systemic agents (e.g., methotrexate and cyclosporine). The guideline writers concluded, "No clinical reason supports reserving the biologicals for second-line use," though the biologics do have their own safety issues.

Other conclusions included:

- Methotrexate is less effective than cyclosporine, but methotrexate can be used for years, while cyclosporine should be used intermittently for periods no longer than 12 weeks at a time.
- Oral retinoid acitretin (**Roche's Soriatane**) has limited efficacy, so it often is used in combination with topical calcipotriene (**Bristol-Myers Squibb's Dovonex**) or phototherapy.
- Patients with hepatitis B virus (HBV) infection should not be given methotrexate or biologics.

ROCHE

- **Avastin (bevacizumab).** In a single-arm Phase II trial presented at the American Society of Clinical Oncology's Multidisciplinary Head and Neck Cancer Symposium, the addition of adjuvant Avastin to chemoradiotherapy improved survival in patients with advanced nasopharyngeal carcinoma. At 2 years, 91% of Avastin patients were alive, and progression-free survival was 75%.
- **Xolair (omalizumab).** The FDA's Pediatric Advisory Committee recommended that monitoring requirements be loosened, requiring only routine monitoring for this subcutaneous injectable drug for moderate-to-severe persistent allergic asthma caused by year-round allergens.

VERTEX PHARMACEUTICALS' Kalydeco (ivacaftor, VX-770) – approved for subset of CF patients

Kalydeco was approved – with just a ~3-month review (half the time of a typical expedited review) – as an orphan drug to treat a rare form of cystic fibrosis (CF) in patients age ≥6 years who have the G551D mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which is ~4% of CF patients (~1,200 people in the U.S).

The twice-daily drug, which is expected to be taken for life (or until a newer, better therapy comes along) will cost $294,000 a year per patient.

CF, which affects about 30,000 people in the United States, is the most common fatal genetic disease in the Caucasian population. If every eligible patient took it – and CF specialists said they would offer it to all eligible patients – the cost to the healthcare system would be ~$353 million a year. However, Vertex said it would provide the drug free to patients with a household income ≤$150,000 without insurance. The company also said it will help with copays regardless of income.

FDA officials were effusive in their praise of this new drug. FDA Commissioner Margaret Hamburg, MD, said, "The unique and mutually beneficial partnership that led to the approval of Kalydeco serves as a great model for what companies and patient groups can achieve if they collaborate on drug development." Janet Woodcock, MD, director of the FDA's Center for Drug Evaluation and Research (CDER), called it a "breakthrough therapy" and blogged about it on the FDA website, praising Vertex's collaboration with the Cystic Fibrosis Foundation to develop and study the drug, "This unique and mutually beneficial partnership that led to the approval of this new therapy for some CF patients serves as a great model for future drug development and patient group collaboration moving forward."

WATSON PHARMACEUTICALS' Ella/Esmya (ulipristal acetate) – possible use for uterine fibroids

Two studies published in the ***New England Journal of Medicine*** suggest this selective progesterone-receptor modulator approved as a morning-after contraceptive may have a new use: treating uterine fibroids without causing hot flashes. One small study found that Ella effectively controlled excessive bleeding and shrank fibroids in women planning to have surgery to remove the growths. After 13 weeks, uterine bleeding was controlled in 91% of women on 5 mg/day and 92% of women on 10 mg/day vs. 19% of placebo patients. Fibroid volume shrank by 21% with 5 mg, shrank 12% with 10 mg, and increased 3% with placebo.

A second, 307-patient study compared Ella to leuprolide acetate. At 3 months, uterine bleeding was controlled in 90% of patients at 5 mg Ella, 98% at 10 mg Ella, and 89% of leuprolide patients. Moderate-to-severe hot flashes did occur but were much less with Ella than with leuprolide: 11% at 5 mg, 10% at 10 mg vs. 40% with leuprolide.

In December 2011, the European Medicines Agency recommended approval of Esmya to be used before fibroid surgery, but final approval has not yet been granted.

REGULATORY NEWS

CMS moves on Power Mobility Device (PMD) pilot

This pilot had been scheduled to start January 1, 2012, but was delayed. The Centers for Medicare and Medicaid (CMS) now says the project will start on or after June 1, 2012. CMS said it "significantly" revised the Prior Authorization of PMDs demonstration in response to provider and supplier concerns. The

pilot requires prior authorization for scooters and power wheelchairs for all people with Medicare who reside in seven states: California, Florida, Illinois, Michigan, New York, North Carolina, and Texas.

CMS issues draft NCD on TAVR

CMS issued its proposed (draft) National Coverage Decision (NCD) for transcatheter aortic valve replacement (TAVR), which will be open for public comment until March 3, 2012. [*Remember TAVR is now the preferred term over TAVI (transcatheter aortic valve implantation).*]

CMS proposes to cover TAVR for patients with severe, symptomatic aortic valve stenosis if these five conditions are ***all*** met:

1. **On-label with FDA-approved device.** The procedure must be an on-label indication, and the device has to have FDA approval for that indication.
2. **Two surgeons review.** Two cardiac surgeons must have evaluated the patient's suitability for surgical valve replacement.
3. **Heart team and expertise required.** The procedure is performed in a facility that meets certain requirements with regard to surgical and interventional cardiology expertise. In addition, institutions with prior TAVR experience must participate in ongoing trials or postmarketing studies, and all centers performing TAVR must commit to the heart team concept and enroll prospective patients in a national TAVR study.
4. **Physicians must be trained.** TAVR must be performed by sufficiently qualified and experienced physicians.
5. **Registry participation mandatory.** The treating team must participate in a national registry that enrolls TAVR patients and tracks the following outcomes: major stroke, all-cause mortality, minor stroke/transient ischemic attack, major vascular events, and acute renal injury.

Under the proposed rules, CMS would cover off-label use of TAVR for aortic valve stenosis only in a clinical trial, and there are 13 conditions for those trials. CMS will not cover TAVR for any other indications, such as mixed aortic-valve disease, isolated aortic regurgitation, untreated clinically significant coronary artery disease requiring revascularization, hypertrophic cardiomyopathy, echocardiographic evidence of intracardiac mass, significant aortic disease, and severe obstructive calcification or tortuosity of the iliofemoral vessel, or small vessel size.

CMS should track doctors who opt out of Medicare

The Department of Health and Human Services' Office of the Inspector General (OIG) told CMS that neither CMS nor Medicare contractors are adequately tracking which physicians are opting out of Medicare and why. The memo said that the OIG could not determine from Medicare records "the characteristics of physicians who opt out of Medicare, the trend in the number of opted-out physicians, or why physicians choose to opt out of Medicare."

However, the OIG believes that the number of physicians opting out increased each year from 2006 to 2010 (the latest year for which there are data). The OIG also is concerned that the rate of opt-outs may increase in the future, especially if physician fees are reduced.

FDA, industry agree on device user fees; now it's up to Congress

The FDA and industry agreed that the FDA should collect $595 million from industry over the next five years in medical device user fees. That amount of money would allow the FDA to hire 200 new people and cut review times.

Reportedly, industry wanted to pay $447 million over the five years, and the FDA wanted $805 million. If they had split the difference, the FDA would have gotten $626 million. On February 15, 2012, the House will hold a hearing on the medical device user fee program, which will expire on September 30, 2012, unless it is reauthorized.

In September 2010, prior to beginning negotiations with regulated industry, the FDA held a public meeting on the device user fee program attended by a variety of stakeholders including industry, scientific, and academic experts, healthcare professionals, and representatives from patient and consumer advocacy groups. Stakeholders provided their assessment of the overall performance of the MDUFA program and their opinions about which aspects of the program should be retained, changed, or discontinued in order to further strengthen and improve the program.

Once the details of the agreement with industry are finalized, the FDA will develop a set of proposed recommendations and put them out for public comment before they are submitted to Congress.

FDA's Dr. Temple off drug development post

CDER chief Dr. Woodcock announced that she is taking oversight of the Office of Drug Evaluation I (ODE I) in the Office of New Drugs away from Robert Temple, MD. Dr. Temple, who has been both Acting Director of ODE I and Deputy Center Director for Clinical Science, will now only keep his Clinical Science duties, which include responsibility for "high-level initiatives and programs related to clinical science and clinical trial methodology." As Dr. Woodcock put it, Dr. Temple will now "have more time to further provide valuable regulatory input and methodological assistance across the Center."

Deputy Director of ODE I, Ellis Unger, MD, is taking over as Acting Director of ODE I. Dr. Unger has been with CDER since 2004, serving in various leadership roles. Dr. Unger is a board-certified internist and has been a drug reviewer for the FDA. In 2009, he was deputy director of the FDA's Division of Cardiovascular and Renal Products, where he was active in the decision on Lilly's Effient (prasugrel). In April 2011, he co-authored a perspective published in the ***New England Journal of Medicine*** with Dr. Temple, explaining the FDA's decision to approve an untested 75 mg dose of Boehringer Ingelheim's Pradaxa (dabigatran).

How well Dr. Unger gets along with Cleveland Clinic cardiologist Steven Nissen, MD, may be a question. Dr. Unger has been quoted as accusing Dr. Nissen of having a "retrospectoscope in his back pocket" and being a "Monday morning quarterback" on Merck's Vioxx (rofecoxib) and GlaxoSmithKline's Avandia (rosiglitazone).

FDA snooping in private emails

Does the FDA have the right to read employees' private emails – and to punish them for what is in those emails? Six doctors and scientists were fired for what the FDA read in their personal email accounts, so the former employees are suing the FDA in federal court. The FDA claims the staffers disclosed information about devices under review, but the Inspector General of the Department of Health and Human Services (HHS) said the staffers had the right to share safety concerns with members of Congress and with reporters.

Sen. Charles Grassley (R-IA) is investigating. He sent a five-page letter to FDA Commissioner Dr. Hamburg demanding to know who authorized the monitoring, how many employees were targeted, whether the FDA obtained passwords to personal email accounts that allowed communications on private computers to be intercepted, and whether this type of surveillance is continuing. He told Dr. Hamburg he is concerned that FDA whistleblowers are "treated like skunks at a picnic."

Legislation would tighten rules on 510(k) submissions

Legislation (HR3847) was introduced by four Democratic members of the House – Rep. Edward Markey (D-MA), Rep. Henry Waxman (D-CA), Rep. Jan Schakowsky (D-IL), and Rep. Rosa DeLauro (D-CT) – that would decrease the number of devices that could be used as predicates for 510(k) submissions. Among the provisions in the bill is a mandate that manufacturers seeking 510(k) clearance submit a market status report, including histories of recalls and corrections, for any devices used as predicates.

The legislation closes a loophole that lets devices be used as predicates even though they've been pulled from the market for safety reasons – e.g., transvaginal mesh.

Maine attempts to limit copay creep

First insurance companies imposed small, flat copays on drugs. Then they tiered drugs, with higher copays for more expensive drugs. Recently, some insurers have imposed percentage copays (technically called co-insurance), sometimes as much as 30%-50%, for specialty drugs. A bill introduced in the Maine legislature would outlaw co-insurance.

FDA approvals/clearances

- **AMYLIN and ALKERMES' Bydureon (exenatide extended-release)** – It took nearly 3 years, but the FDA finally approved this once-weekly injectable GLP-1 receptor agonist for Type 2 diabetes. The FDA mandated a Risk Evaluation and Mitigation Strategy (REMS) to address concerns about potential acute pancreatitis and medullary thyroid cancer, and the company must conduct post-marketing trials to study those adverse events as well as cardiovascular effects. The cost: ~$350/month.
- **BOEHRINGER INGELHEIM and LILLY's Jentadueto (linagliptin + metformin)** was approved to treat Type 2 diabetes.
- **BOVIE MEDICAL's J-Plasma** handpiece with a retractable cutter for soft tissue coagulation during surgical procedures was given 510(k) clearance.
- **CARL ZEISS MEDITEC's Cirrus HD-OCT** software upgrade for diagnosing dry age-related macular degeneration (AMD) and glaucoma was cleared by the FDA.

- **DISCOVERY LABORATORIES' Afectair**, a disposable ventilator circuit/patient interface connector that simplifies the delivery of aerosolized medications to critical-care patients requiring ventilatory support, was cleared for use.
- **MERCK's Janumet XR (extended-release sitagliptin + metformin)** was approved.
- **NOVARTIS' Gleevec (imatinib)** was granted expanded use in adult patients following surgical removal of CD117-positive gastrointestinal stromal tumors (GIST).
- **ROCHE/GENENTECH and CURIS' Erivedge (vismodegib)**, a once-daily, oral hedgehog pathway inhibitor, was approved as the first drug for locally advanced and metastatic basal cell carcinoma. It will be available only through specialty pharmacies, and it will have a boxed warning about teratogenicity.
- **TEARSCIENCE's LipiFlow** – An updated version that allows patients with evaporative dry eye to receive treatment for both eyes simultaneously received 510(k) clearance.
- **TOSHIBA AMERICA MEDICAL SYSTEM's Aquilion Prime CT scanner** received 510(k) clearance.
- **VERTEX PHARMACEUTICALS' Kalydeco (ivacaftor, VX-770)** was approved to treat a subset of cystic fibrosis patients (*for details see page 4*).

FDA recalls/warnings

- **BEDFORD LABORATORIES** voluntarily recalled one lot of acetylcysteine solution due to glass particles in a vial.
- **PFIZER's Lo/Ovral-28 (norgestrel/ethinyl estradiol)** – Pfizer recalled 1 million packs (14 lots of the brand plus another 14 lots of a generic version) of these birth control pills after discovering that some blister packs had the incorrect number of pills and in other packages the pills were in the wrong order. Either situation could make them ineffective. The pills were manufactured and packaged by Pfizer but were marketed by **Akrimax Rx Products** under the **Akrimax Pharmaceuticals** brand.

European regulatory actions

- **CELATOR PHARMACEUTICALS' CPX-351 (liposomal cytarabine + daunorubicin)**, a treatment for acute myeloid leukemia (AML), was granted orphan drug status.
- **CHARTER MEDICAL's cryogenic stem cell containers** received a CE Mark to store, preserve, and transfer hematopoietic stem cells.
- **MINVASYS' Danubio drug-coated coronary balloon** received a CE Mark.
- **SERVIER** – The European Commission dropped its complaint alleging that Les Laboratoires Servier gave misleading information during an investigation into a practice that delays generic-drug launches. The commission said it will focus on pending antitrust cases against several drugmakers, including Servier.

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

JOHNSON & JOHNSON's Zytiga (abiraterone) – This prostate cancer drug, which was discovered in England and developed with funds from U.K. charities, was deemed too expensive for the National Health Service, which said the drug's benefits don't justify the cost (~$4,750/month) even after J&J agreed to a price cut.

Other regulatory news

Mexican regulator Cofepris signed an agreement with Japan similar to the ones it has with the U.S. and Canada for expedited review in Mexico of devices approved as Class II, III, or IV in Japan.

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 7	FDA's proposed **user fees for biosimilars**	Health subcommittee of House Energy and Commerce Committee hearing
February 8	**Amgen's Xgeva** (denosumab) for prevention/delay of bone metastases in castration-resistant prostate cancer	FDA's Oncologic Drugs Advisory Committee (ODAC)
February 9	**Eisai's Dacogen** (decitabine) for treatment of acute myelogenous leukemia (AML)	FDA's Oncologic Drugs Advisory Committee
February 9	**NeurogesX's Qutenza** (transdermal capsaicin) for HIV-related neuropathic pain	FDA's Anesthetic and Analgesic Drugs Advisory Committee
February 10	Possible reclassification of **cranial electrotherapy stimulator (CES) devices** to Class III (requiring a PMA)	FDA's Neurological Devices Advisory Committee
February 15	Reauthorization of **FDA user fee program for medical devices**	Health subcommittee of House Energy and Commerce Committee hearing
February 17	**Corcept Therapeutics' Corlux** (mifepristone) for Cushing's syndrome	PDUFA date
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	Review of evidence needed for approval of **anti-inflammatory ophthalmic drugs post-ocular surgery** and appropriateness of marketing a single bottle for use in both eyes post-surgery	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 7	**NeurogesX's Qutenza** (transdermal capsaicin) for neuropathic pain	PDUFA date
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 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
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
	April 2012	
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 26	**Amgen's Xgeva** (denosumab) for prevention/delay of bone metastases in castration-resistant prostate cancer	PDUFA date
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
2Q1	**Arena Pharmaceutical and Eisai's Lorqess** (lorcaserin) for weight loss	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**
	Other 2012	
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
June	**Forest Laboratories and Ironwood Pharmaceuticals' linaclotide** for IBS-C	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