TRENDS-in-MEDICINE

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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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NOTE: Subscribe to *Trends-in-Medicine* for full coverage of Digestive Disease Week (DDW).

SHORT TAKES

- **ACHILLION PHARMACEUTICALS' ACH-3102**, a second-generation NS5A inhibitor, was granted fast track status by the FDA, which means the company can do a rolling submission for this oral hepatitis C drug.

- **AGILENT TECHNOLOGIES**, which makes scientific testing equipment, is buying **Dako**, a Danish company that makes cancer-diagnostics tools. This is the largest purchase in Agilent's history.

- **BG MEDICINE's BGM Galectin-3 –** The company applied to the FDA for an expanded 510(k) clearance for use of this test in the general adult population. It already has clearance as an assay to identify chronic heart failure patients who are at a greater risk for death or hospitalization.

- **CARDINAL HEALTH** is acquiring **Dik Drug Co.**, a privately held regional drug wholesaler.

- **DENDREON's Provenge (sipuleucel-T) –** The Securities and Exchange Commission (SEC) is investigating whether the company misled investors about this prostate cancer therapy by giving overly optimistic projections of adoption.

- **Gene therapy –** A Phase I study by Taiwanese researchers, with the help of University of Florida researchers, published in the journal ***Science Translational Medicine***, reported that gene transfer technology restored some movement in four children bed-ridden with a rare, incurable brain disease caused by a gene deficiency. The researchers used an adeno-associated virus Type 2 vector to transport the missing genes into the putamen area in the brains of the children. Eight additional children – four in Taiwan and four in the U.S. – are expected to receive the experimental treatment.

- **GLAXOSMITHKLINE's Treximet (sumatriptan + naproxen) –** A 12-week study published in ***Pediatrics*** found that this combination tablet relieves migraines in adolescents (age 12-17) as well as in adults. In the study, 23%-29% of Treximet patients vs. 10% of placebo patients were pain-free within two hours.

- **HEARTWARE's HVAD –** The FDA told investigators that it is not sanctioning the NIH-sponsored REVIVE-IT trial of this left ventricular assist device in NYHA Class III heart failure patients, saying it is too risky for a less advanced patient population (patients not severe enough to qualify for transplant or LVAD therapy based on current guidelines) – at least as the trial is currently designed.

- **JOHNSON & JOHNSON's Zytiga (abiraterone)** – NICE originally determined this oral prostate cancer treatment was not cost-effective, but NICE has now reversed itself and approved use.

- **LUNDBECK and TAKEDA's vortioxetine (Lu AA21004)** – The company reported that Phase III trial results for this investigational antidepressant were strong enough that it will submit the drug for approval to U.S., European, and Canadian regulators.

- **MEDTRONIC's Infuse (recombinant human bone morphogenetic protein-2, rhBMP-2)** – The company announced that the Department of Justice and the U.S. Attorney's Office in Massachusetts have closed their investigation into the off-label use of this bone graft product for spinal fusions without any charges or any penalties. *After a four-year investigation, it looks like Medtronic was cleared of any wrongdoing!*

- **MOLOGEN's MGN-1703** – The company said this investigational immunomodulator slowed the spread of colorectal cancer in a Phase II trial, doubling survival vs. placebo.

- **NOVARTIS' glycopyrronium bromide (NVA-237)** – The company announced that a Phase III trial showed this inhaled long-acting muscarinic antagonist to be superior to placebo and similar to **Pfizer** and **Boehringer Ingelheim's Spiriva** (tiotropium) in improving lung function. The full results are being presented at the American Thoracic Society meeting.

- **OMNICARE** agreed to pay $50 million to settle Department of Justice charges, arising out of a Drug Enforcement Administration (DEA) investigation, that it failed to properly oversee distribution of controlled substances at some of its pharmacies. The issue was how pharmacy managers communicated with doctors writing prescriptions for controlled substances used in long-term care facilities. This is reported to be the second-largest civil settlement in the history of the Controlled Substances Act.

- **ORASURE TECHNOLOGIES' OraQuick In-Home HIV Test** – The FDA's Blood Products Advisory Committee voted unanimously (17-0) to recommend approval of this over-the-counter HIV test, concluding that the benefits outweigh the potential risks. While the panel noted that it probably isn't as accurate as a professionally administered diagnostic test, patients might be more willing to test themselves.

- **PHYTOPHARM's Myogane (PYM-50018)** – The company reported that a preclinical study in an animal model of glaucoma failed to show any significant improvement in neuronal cell loss, a marker of the disease.

- **PIRAMAL HEALTHCARE**, an Indian firm, is buying **Decision Resources Group**, a U.S. healthcare information company that does research and analysis for pharmas.

- **SANOFI's Plavix (clopidogrel)** is now off-patent. And the FDA immediately approved generics of this blood thinner by Gate Pharmaceuticals, Mylan Pharmaceuticals, Dr. Reddy's Laboratories, and Teva for a 300 mg dose plus Apotex, Aurobindo Pharma, Mylan Pharmaceuticals, Roxane Laboratories, Sun Pharma, Teva, and Torrent Pharmaceuticals for a 75 mg dose.

- **TGF-beta** – In research published in the ***Journal of Immunology***, Loyola University researchers reported that they may have found a new target for regulating the immune system – transforming growth factor beta (TGF-β) – which could lead to new drugs to regulate the immune system by either revving it up to attack tumor cells or tamping it down to prevent the rejection of transplanted organs.

- **TOWERS WATSON & CO.** is buying **Extend Health**, which operates the largest private Medicare exchange in the U.S. (a health insurance exchange or HIE). The new business segment will be called **Exchange Solutions**.

- **U-SYSTEMS' somo-v Automated Breast Ultrasound (ABUS) system** – The FDA issued an "approvable" letter for this automated breast ultrasound system, designed as an adjunct to mammograms for women with dense breasts. The company expects premarket approval once its manufacturing sites pass an audit. In April, the FDA's Radiological Devices Advisory Committee unanimously recommended approval.

NEWS IN BRIEF

ASCO preview news

American Society of Clinical Oncology (ASCO) officials held a webcast for reporters to highlight some of the trials that will be reported in greater detail at the annual ASCO meeting in June 2012. Michael Link, MD, a pediatric oncologist from Stanford University and ASCO president, said the two themes this year are "precision medicine" and a move away from treating cancer based on body part or organ site to more focus on genetics and mutation drivers. Other publications may report on data from ASCO abstracts to be presented at the meeting, but those are not the final results, and ***Quick Takes*** will not report on them unless they are confirmed.

Among the trials:

- **GLAXOSMITHKLINE's dabrafenib (GSK-2118436) – adding a MEK inhibitor boosts efficacy, cuts side effects.** Updated safety and efficacy results from a Phase I/II trial in BRAF-naïve metastatic melanoma found that combining this BRAF inhibitor with the oral MEK inhibitor trametinib (GSK-1120212) reduced the incidence of skin rash and squamous cell carcinoma normally seen with BRAF inhibitors while also boosting the efficacy (overall response rate of 63%). Progression-free survival (PFS) of 10.8 months was reported for a dose of 150 mg BID dabrafenib + 2 mg QD trametinib, and that is the regimen that will be used in Phase III.

- **JOHNSON & JOHNSON's Zytiga (abiraterone) – positive neoadjuvant prostate cancer results.** A small, randomized, Phase II study in newly diagnosed, high-risk prostate cancer patients found that using abiraterone earlier in the disease – neoadjuvant therapy – appears to be beneficial, the low dose of prednisone is sufficient, and six months of the drug appears to be much better than just three months.

- **LILLY's Zyprexa (olanzapine) – good anti-emetic and anti-nausea drug for cancer patients.** An 80-patient study found that a short course of this antipsychotic (10 mg daily for 3 days) is more effective than metoclopramide (10 mg TID for 3 days) in reducing chemotherapy-induced nausea and vomiting (CINV). Researchers believe it is probably a class effect, though that needs to be proved.

- **PFIZER's Xalkori (crizotinib) – appears effective in ALK-positive cancers other than lung.** A Phase I study found that this ALK-inhibitor – which is FDA-approved to treat ALK+ lung cancer – is effective in treating children with relapsed/refractory ALK-driven anaplastic large cell lymphoma (ALCL) and **may** be beneficial in neuroblastoma and inflammatory myofibroblastic tumors.

  The study determined that 280 mg/m^2/day is the recommended Phase II dose. While the ALCL data were convincing enough to move to Phase III, more Phase II work needs to be done in the other pediatric cancers.

BOSTON SCIENTIFIC

- **Sadra Lotus – positive early results.** The results of the prospective, single-arm, 11-patient REPRISE-I feasibility trial conducted in Australia of this repositionable 23 mm transcatheter aortic valve, delivered on an 18Fr catheter, showed that nine valves were successfully delivered. One of the failures was a patient who had a major ischemic stroke. Investigators reported no moderate or severe paravalvular leaks either immediately after implantation or at discharge. The 120-patient REPRISE-II trial is expected to start later this year in Australia and Europe, testing both a 23 mm and a 27 mm valve. A pivotal trial for a CE Mark is expected to start in 2013.

- **Watchman – positive registry results.** The results of the non-randomized, 150-patient ASA Plavix Registry were reported at the Heart Rhythm Society meeting, showing that this left atrial appendage closure device, when used with aspirin and clopidogrel, prevents strokes in atrial fibrillation (AFib) patients unable to take warfarin.

  At 2 years, Watchman patients had an annual ischemic stroke rate of 1.7%, which compares to an expected stroke rate of 7.3%. However, 3.3% of Watchman patients had a thrombus (without serious consequences), 2% had pericardial effusion with tamponade, 1.3% had device embolization, and 2.7% had major bleeding.

  Watchman, developed by **Atritech** (which was acquired by Boston Scientific in 2011), has a CE Mark but has not yet been approved by the FDA, despite a positive advisory committee recommendation in 2009, because of concerns about pericardial effusion. The FDA wanted another trial, and PREVAIL reportedly has nearly completed enrollment. The registry looks at a different group of patients – those with contraindications to warfarin.

CARDINAL vs. DEA – DEA wins

Under the settlement reached with the Drug Enforcement Administration, Cardinal Health's license to distribute controlled substances, including opioids, from its Lakeland FL distribution center is suspended for two years, and during that period it cannot ship controlled substances out of the facility. In addition, Cardinal must implement improved procedures to prevent diversion.

Colonoscopy – virtual as good as optical for large polyps

A prospective, 605-patient study published in the ***Annals of Internal Medicine*** found that virtual colonoscopies – laxative-free, computer-aided CT scans – appear similar to optical colonoscopy in detecting larger adenomas but are not as good at finding smaller lesions. The virtual colonoscopies identified 91% of adenomas ≥10 mm vs. 95% identified by standard optical colonoscopy. Most polyps that impact cancer and survival are that size. However, virtual colonoscopies had significantly less sensitivity and specificity for detecting polyps of 6-8 mm.

Virtual vs. Optical Colonoscopy			
Measurement	**Virtual**	**Optical**	**p-value**
Sensitivity			
≥10 mm adenoma	0.91	0.95	Nss, 1.00
≥8 mm adenoma	0.70	0.88	Nss, 0.124
≥6 mm adenoma	0.59	0.76	Nss, 0.06
Specificity			
≥10 mm adenoma	0.85	0.89	Nss, 0.08
≥8 mm adenoma	0.86	0.91	0.02
≥6 mm adenoma	0.88	0.94	0.001

EuroPCR news

The news from this interventional cardiology meeting in Paris included:

- ***Is interventional cardiology branching out into neurosurgery?*** Jacques Moret, MD, argued that interventional cardiologists and interventional vascular radiologists have the ideal background, in terms of endovascular skill and training, to support interventional neuroradiologists in providing 24-hour coverage for stroke patients who need mechanical thrombectomy of cerebral arteries. Dr. Moret noted that there is a shortage of interventional neuroradiologists in many European countries, and training more will take a long time, so he suggested training interventional vascular radiologists and interventional cardiologists to fill the gap, at least until there are enough dedicated interventional neuroradiologists.

- **BIOSENSORS' BioMatrix Flex stent** – Patrick Serruys, MD, from the Netherlands announced plans to start a large (~16,000-patient) investigator-driven, all-comers trial, GLOBAL LEADERS, later this year. The trial will compare two antiplatelet strategies in drug-eluting stent (DES) patients. Patients getting the BioMatrix Flex stent, a DES with an albuminally coated biodegradable polymer, will be randomized to **AstraZeneca's Brilinta** (ticagrelor) for 24 months (+ aspirin only for the first month) vs. a 12-month course of dual antiplatelet therapy (clopidogrel + aspirin), followed by 12 additional months of aspirin monotherapy.

- **EDWARDS LIFESCIENCES' Sapien** – The 30-day results from a European registry of 2,706 patients showed that the Sapien XT, a second-generation transcatheter aortic valve, had mortality of 6.3% (4.3% transfemoral and 9.9% transapical). While these are all lower than seen in the SOURCE registry of the first-generation Sapien, these are also less sick patients. However, the rate of major bleeding and new pacemaker use was higher with Sapien XT.

  In addition, first-in-man data on the repositionable **Sapien 3**, the company's next-generation balloon expandable transcatheter aortic valve were presented. None of the 12 patients died, had a major stroke/bleeding event, or major vascular complications, and only one patient required a permanent pacemaker. There were 2 cases of paravalvular (PV) leak. A CE Mark trial is expected to start later this year.

  And there were data on Edward's new **Centera** self-expandable valve with a motorized delivery system. It obviously is not yet ready for prime time. At 30 days, 4 of the 10 patients required a permanent pacemaker, though a new delivery system may help reduce that number. A CE Mark trial of this valve also is expected to start later this year.

- **Fractional flow reserve (FFR)** – Percutaneous coronary intervention (PCI) guided by FFR was shown in the FAME-II trial to reduce the need for revascularization by a factor of up to 11 by targeting stenting to ischemic patients and giving the others optimal medical therapy alone.

- **ST. JUDE MEDICAL's EnligHTN – positive results and European approval.** The 30-day results of the single-arm, non-randomized, 47-patient, first-in-man EnligHTN-I trial of this renal denervation (RDN) system for resistant hypertension were presented.

  The study found that, on average, the procedure reduced systolic blood pressure (SBP) by 28 mmHg (from 176 to 148) and diastolic blood pressure (DBP) by 10 mmHg (from 96 to 86) in patients with hypertension (mean 176/96) despite taking an average of four antihypertensive medications. In addition, 41% of patients achieved SBP of <140 mmHg.

  The procedure took an average of 34 minutes, and there were no serious complications. EnligHTN received European approval on May 15, 2012, and was launched, making it the fifth renal denervation system on the European market but the only multi-electrode ablation technology. FDA approval is expected in 2016.

  There were also data and presentations on other investigational renal denervation systems at EuroPCR. Renal denervation quite simply was a hot topic at the meeting.

NOVARTIS' Gilenya (fingolimod) – new FDA safety warning and limitations on use

The FDA issued another safety warning about this oral multiple sclerosis (MS) drug, revising upward its recommendations for cardiovascular monitoring. After completing its review of one patient death and other reports of patients who died of cardiovascular or unknown causes, the FDA decided it could not definitively conclude that Gilenya was responsible for any

of the deaths, but the Agency is still concerned about the cardiovascular effects of Gilenya after the first dose. The FDA said the data show that the maximum heart rate-lowering effect of Gilenya ***usually*** occurs within 6 hours of the first dose, but the maximum effect may occur as late as 20 hours after the first dose.

Thus, the FDA now contraindicates Gilenya in patients with certain pre-existing or recent (within last 6 months) heart conditions or stroke or who are taking certain antiarrhythmic medications. And the FDA continues to recommend that all patients starting Gilenya be monitored for signs of bradycardia for at least 6 hours after the first dose.

The FDA has added a recommendation that doctors monitor hourly pulse and blood pressure measurements for all patients starting Gilenya. And the FDA is now recommending that the length of cardiovascular monitoring be extended beyond 6 hours in high-risk patients, and this should include continuous EKG monitoring overnight.

PFIZER's Zithromax (azithromycin) – study cites increased risk of sudden death

A study by Vanderbilt University researchers published in the ***New England Journal of Medicine*** found a small increase in the risk of sudden death in adults, especially patients who have heart disease or are at high risk for it, with this macrolide antibiotic. The researchers analyzed the Tennessee Medicaid database for a 14-year period and found sudden deaths were rare, but the rate was more than twice as high with azithromycin vs. amoxicillin.

The FDA immediately issued a safety alert, notifying doctors that it is aware of the study, is reviewing the results, and will communicate any new information on azithromycin, the study, or the potential risk of QT interval prolongation when it completes its review. The Agency also noted that there is already a warning in the label of macrolides about possible QT prolongation and torsades de pointe and updated as recently as March 2012.

REGULATORY NEWS

CDC wants all baby boomers tested for HCV

Baby boomers reportedly account for 75% of all the Americans infected with the hepatitis C virus (HCV), so the Centers for Disease Control and Prevention (CDC) is recommending that everyone age 47-67 be tested for HCV, even if they don't have risk factors for the disease.

The CDC said one-time HCV testing of everyone in this age group could identify >800,000 additional people with HCV, prevent liver cancer and other chronic liver diseases, and save lives.

ESC issues new heart failure guidelines

The European Society of Cardiology (ESC) launched new guidelines for the diagnosis and treatment of acute and chronic heart failure at the Heart Failure Congress in Serbia, and they were published in the ***European Heart Journal***.

Among the changes are:

- Left ventricular assist devices (LVADs) are recognized as possible destination therapy, not just bridge-to-transplant.
- Cardiac resynchronization therapy (CRT) is now indicated for some patients with mild symptoms as well as more severe patients.
- Transcatheter aortic valves are discussed, and the guidelines indicate they can be appropriate for aortic stenosis patients who are unsuitable for surgery.
- Beta blockers are the recommended first-line therapy, and doses should be maximized before adding additional medications to reduce hypertension.
- For hypertension, standard therapy for many patients should include three drug classes – a beta blocker, an ACE inhibitor or ARB, and a mineral corticoid receptor antagonist – as well (e.g., spironolactone or eplerenone).
- Pro-A-type natriuretic peptide is mentioned for the first time as a diagnostic.

FCC to dedicate bandwidth for medical devices

Federal Communications Commission (FCC) chairman Julius Genachowski announced that his agency is likely to dedicate a nationwide swath of spectrum to the operation of wireless medical monitoring devices. This would allow Medical Body Area Networks to be created by hospitals, clinics, and doctors, and it is likely to spur use of disposable, wireless sensors in those environments. Final approval is expected at the FCC's open meeting on May 24, 2012.

FDA drug approval faster than Europe or Canada

A Yale University study published in the ***New England Journal of Medicine*** found that the FDA actually approved drugs >3 months faster than Health Canada or the European Medicines Agency (EMA). The study found that 64% of novel drugs approved in both the U.S. and in Europe had been

approved by the FDA first, and 86% of medicines approved in both the U.S. and Canada had been approved first in the U.S.

HHS considers national health information network

The Department of Health and Human Services (HHS) is seeking public comment on how to run a nationwide health information network that would allow medical data to be shared quickly online as a way to lessen duplicative testing, reduce medical errors, and promote teamwork in the delivery of healthcare, calling it "an opportune time" to solicit input on how a nationwide health information network should be shaped. Officials added that it is a good time to see "how we could effectively use our statutory authority to complement existing federal regulations."

NIH to fund two Alzheimer's trials

National Institutes of Health (NIH) Director Francis Collins, MD, speaking at an Alzheimer's conference, said that NIH has two large-scale clinical trials already underway, including the first prevention trial, and early results could be available later this year.

- **ROCHE/GENENTECH's crenezumab (RG-7412)** – A 5-year prevention trial focusing on an extended family of ~5,000 Colombians, some of whom have a genetic mutation that predisposes them to exhibit signs of Alzheimer's by age 45 or even earlier, testing when this humanized monoclonal anti-beta-amyloid antibody (licensed from AC Immune) can delay the onset of the disease.
- **A nasal spray to deliver insulin to the brain** – This 240-patient study will test whether delivering insulin this way can improve memory function in people with mild cognitive impairment and early Alzheimer's disease.

FDA approvals/clearances

- **BIOTRONIK's Lumax 740**, next-generation implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT-D) devices for treating patients with heart failure, was cleared for use.
- **COVALON TECHNOLOGIES' IV Clear**, an antimicrobial silicone adhesive film dressing used to secure vascular intravenous access devices, was cleared for use to reduce catheter-based bloodstream infections.
- **GLAXOSMITHKLINE/STIEFEL's Fabior (tazarotene foam)**, a topical retinoid, was approved to treat acne vulgaris.
- **IDAHO TECHNOLOGY's FilmArray Respiratory Panel** received 510(k) clearance for use with five new pathogens, including *Bordetella pertussis* and *Chlamydophila pneumoniae*.

FDA recalls

HOSPIRA's hydromorphone injection – One lot of this injectable painkiller was recalled because it may contain too much drug.

European regulatory actions

- **BOSTON SCIENTIFIC's Innova**, a self-expanding stent for peripheral vascular lesions in arteries above the knee, received a CE Mark.
- **GLAUKOS iStent** – In October 2011 the company lost its CE Mark for this glaucoma drainage device. The Notified Body concerned – Det Norske Veritas (DNV), based in Norway – withdrew the CE certificate, but it is not yet clear why.
- **HYPERBRANCH MEDICAL TECHNOLOGY's Adherus AutoSpray Dural Sealant** received a CE Mark for use in preventing cerebrospinal fluid leaks after a cranial or spinal surgical procedure.
- **ST. JUDE MEDICAL's EnligHTN**, a multi-electrode ablation system for renal denervation, was approved and launched to treat resistant hypertension.

Other regulatory actions

Canada: **OSIRIS THERAPEUTICS' Prochymal**, a stem cell therapy, was approved by Health Canada to treat children suffering from graft-vs.-host disease, a potentially deadly complication of bone marrow transplantation. Prochymal is manufactured by taking mesenchymal stem cells from the bone marrow of healthy young adult donors and then expanding them in culture, so that one donation can make up to 10,000 doses. The company plans to submit Prochymal to the FDA later this year.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	May 2012	
May 23	**Johnson & Johnson's Xarelto** (rivaroxaban), an anticoagulant for a supplemental indication in acute coronary syndrome (ACS)	FDA's Cardiovascular and Renal Drugs Advisory Committee
May 24	**St. Jude Medical's Amplatzer** and **Gore's Helex ASD Occluder** for atrial septal defect closure – discussion of current safety and effectiveness for these devices, first approved in 2001 and 2006, respectively	FDA's Circulatory System Devices Advisory Committee
May 24	**Pfizer/FoldRx Pharmaceuticals' Vyndaqel** (tafamidis meglumine) for the treatment of transthyretin (TTR) familial amyloid polyneuropathy	FDA's Peripheral and Central Nervous System 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 2012	
June 5	**Merck/Ariad Pharmaceuticals' Taltorvic** (ridaforolimus) for sarcoma	PDUFA date
June 8	**Roche/Genentech's pertuzumab** in HER2+ advanced breast cancer	PDUFA date
June 13	**Edwards Lifesciences' Sapien** transcatheter aortic valve repair (TAVR), an expanded indication for high-risk, operable patients	FDA's Circulatory System Devices Advisory Committee
June 15	**Gilead Sciences' Truvada** (emtricitabine + tenofovir) for HIV prevention	PDUFA date
June 20	**Onyx Pharmaceuticals' carfilzomib**, a treatment for relapsed and refractory multiple myeloma	FDA's Oncologic Drugs Advisory Committee (ODAC)
June 21	**Dune Medical Devices' MarginProbe System**, which uses electro-magnetic waves to characterize human tissue in real time and provides intraoperative information on a malignancy of the surface of an *ex vivo* lumpectomy specimen	FDA's General and Plastic Surgery Devices Advisory Committee
June 21	**Repligen's RG-1068**, an imaging agent to help identify abnormalities in pancreatic ducts	PDUFA date
June 25	**QRxPharma's MoxDuo** (morphine + oxycodone) for pain	PDUFA date
June 27	**Arena Pharmaceuticals and Eisai's Lorqess** (lorcaserin) for obesity	PDUFA date
June 27	**Onyx Pharmaceuticals' carfilzomib**, a treatment for relapsed and refractory multiple myeloma	PDUFA date
June 27-28	Risk:benefit of **metal-on-metal hip replacement** and **resurfacing**	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee
June 28	**Bristol-Myers Squibb's Eliquis** (apixaban), an anticoagulant for the prevention of stroke in Afib	PDUFA date
June 29	**Astellas Pharma's Betanis** (mirabegron) for treatment of overactive bladder	PDUFA date
	July 2012	
July 17	**Vivus' Qnexa** (phentermine + topiramate) for weight loss	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 27	**Salix Pharmaceuticals and Progenics Pharmaceuticals' Relistor** (subcutaneous methylnaltrexone bromide) for chronic pain not caused by cancer	PDUFA date
July 30	**Regeneron's Arcalyst** (rilonacept) for gout	PDUFA date
July 30	**Almirall and Forest Laboratories' aclidinium** inhaled therapy for chronic obstructive pulmonary disease (COPD)	PDUFA date
	August 2012	
August 4	**Regeneron Pharmaceuticals** and **Sanofi's Zaltrap** (aflibercept) for colon cancer	PDUFA date
August 12	**Talon Therapeutics' Marqibo** (vincristine sulfate liposomes injection) for Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL)	PDUFA date (extended from May 13)
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

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
Other 2012		
September 5	**Salix Pharmaceuticals' Provir** (crofelemer) for HIV-related diarrhea	PDUFA date (extended from June 5)
September 8	**Ironwood Pharmaceuticals and Forest Laboratories' linaclotide** for irritable bowel syndrome	PDUFA date
September 10	**Navidea Biopharmaceuticals' Lymphoseek**, a radioactive agent for tracing lymph nodes in cancer patients	PDUFA date (extended from June 10)
September 23	**Regeneron's Eylea** (aflibercept) for central retinal vein occlusion (CRVO)	PDUFA date
October 21	**Impax Laboratories' IPX-066** for Parkinson's disease	PDUFA date
October 29	**Cornerstone Therapeutics' CRTX-080** to treat hyponatremia	PDUFA date