TRENDS-in-MEDICINE

June 19, 2011

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…

SHORT TAKES

- **ABBOTT LABORATORIES' Duodopa (levodopa/carbidopa intestinal gel)** – The company said preliminary results from a Phase III trial showed this drug decreases the time before which a Parkinson's disease patient's symptoms returned as well as increases the time during which dyskinesias were well managed.

- **ACTAVIS** is seeking an emerging-market partner to help it copy complicated biosimilar medicines, and one target is **Roche**'s Avastin (bevacizumab). Actavis might start development in emerging markets because clinical trials are not required there.

- **ACUSPHERE's Imagify Perflubutane Polymer Microspheres for Injectable Suspension** – This specialty pharma reached an agreement with the FDA on a non-binding Special Protocol Assessment (SPA) trial of 900 patients, assessing the ability of this imaging agent to detect coronary artery disease (CAD) on stress ultrasound vs. normal stress ultrasound.

- **Atypical antipsychotics** – A study in the journal ***Sleep Medicine*** compared atypical antipsychotic use in 84 patients with a variety of mental health disorders (e.g., depression, bipolar disorder, psychosis) to 331 mentally healthy controls and 221 patients with depression, finding that atypical antipsychotics use was associated with a significant increase in the risk of obstructive sleep apnea in patients with depression.

- **BIONDVAX PHARMACEUTICALS' Multimeric-001** – The company announced the first part of a 200-patient Phase II trial of this universal flu vaccine in healthy adult volunteers met the primary endpoints of safety and immunogenicity. The company also said that adding Multimeric-001 to a strain-dependent seasonal flu vaccine enhanced the traditional, commercially available vaccine's performance. The second part of the trial will test the vaccine in elderly patients.

- **CADENCE PHARMACEUTICALS' Ofirmev (IV acetaminophen)**, an analgesic for mild-to-moderate pain, has been added to the Department of Defense's formulary and can be prescribed to members of all four military branches in U.S. and overseas military hospitals as well as combat theaters.

- **CATALYST PHARMACEUTICAL PARTNERS' CPP-115**, a treatment for infantile spasms, reduced observed spasms three times longer than standard treatment in a preclinical trial. The drug has orphan drug status.

- **COMPASS INTERNATIONAL INNOVATIONS**, a maker of stereotactic position devices, received a warning letter from the FDA saying that, among several violations, it failed to set up procedures for validating software used in its surgical systems.

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- **COVIDIEN** has put its pharmaceuticals business on the market. One deal apparently has fallen through, but Covidien is looking for another buyer.

- **CUBIST PHARMACEUTICALS' CXA-201 –** The company announced this antibiotic met the primary endpoint in a 122-patient, Phase II trial in complicated abdominal infections, with efficacy nearly as good as AstraZeneca's antibiotic Merrem (meropenem). Cubist plans to move into Phase III testing as a treatment for complex infections of the urinary tract and abdomen by the end of 2011.

- **CYPRESS PHARMACEUTICALS' Zutripro (hydrocodone + chlorpheniramine + pseudoephedrine) and Rezira (hydrocodone + pseudoephedrine) –** The FDA approved these oral solutions to treat coughs and colds, making them the only approved products that combine the painkiller hydrocodone and a nasal decongestant. Both drugs were designated controlled substances.

- **DR. REDDY'S LABORATORIES –** The FDA found four violations at a Mexican plant of Dr. Reddy's subsidiary **Industrias Quimicas Falcon de Mexico**, which makes active pharmaceutical ingredients and intermediates. In a warning letter, the FDA said it might not allow sale or importation of products made at the facility until the issues are resolved.

- **EDISON PHARMACEUTICALS' EPI-743** received orphan drug status from the FDA as a treatment for inherited respiratory chain disorders of the mitochondria.

- **ENZO BIOCHEM** is acquiring the marketing rights to a human papillomavirus (HPV) test developed by **IncellDx** that is designed to assess the likelihood that a patient with HPV will develop cervical cancer. Regulators have not yet cleared the test, and Enzo said it will conduct studies of the test before seeking New York State approval.

- **Epilepsy drugs –** A study published in the ***British Journal of Obstetrics and Gynecology*** found that women with epilepsy are more likely to have pregnancy complications, including a doubled risk of preeclampsia.

- **GILEAD SCIENCES –** In an investigation of the company's manufacturing and distribution, the U.S. Attorney for the Northern District of California subpoenaed information on several products, including pulmonary drug Letairis (ambrisentan) and HIV drugs Atripla (efavirenz + tenofovir + emtricitabine), Truvada, and Hepsera (adefovir).

- **Glaucoma –** A study of 1,404 patients published in the ***Archives of Ophthalmology*** found average per patient spending on glaucoma medications in the U.S. increased overall from $445 in 2001 to $557 in 2006. The change was driven by increased spending by women, patients with public insurance, and patients with less than a high school education.

- **GLAXOSMITHKLINE's Rotarix –** A large study from Mexico and Brazil found that this rotavirus vaccine was associated with intussusception, a potentially life-threatening bowel disorder. The researchers estimated that 1:51,000 to 1:68,000 vaccinated babies will get intussusception. The study also confirmed that the risk of bowel obstruction was ***not*** limited to the withdrawn vaccine. However, the researchers concluded that the benefits of vaccination far exceed the risks.

- **IMPAX LABORATORIES –** The FDA issued a warning letter to Impax after inspectors found deficient sampling and testing procedures at the company's Hayward CA plant. Impax is still being allowed to ship products, but the company said new drug approvals could be affected.

- **INSULET** acquired **Neighborhood Diabetes**, a medical equipment distributor of diabetes supplies.

- **LUNDBECK's nalmefene –** The company said this drug to treat alcohol dependence performed well in three clinical trials, and the company plans to submit the drug to European regulators but not to the FDA because of weak patent protection in the U.S.

- **MAQUET DATASCOPE's Intra-Aortic Balloon Pumps (IABPs) –** These devices to provide temporary left ventricle support during cardiac surgery were recalled because a defective fan in the power supply might cause overheating and shut down the device without visible or audible alarms.

- **MCKESSON –** The Michigan attorney general alleged in a lawsuit that McKesson and **Hearst** conspired to inflate average wholesale drug prices by up to 5% (*yes, 5%*), causing the Michigan Medicaid program to overpay pharmacy claims for eight years.

- **MERCK SERONO** signed an exclusive licensing agreement with **Affectis Pharmaceuticals** for development of oral compounds targeting the P2X7 receptors, which are believed to play a role in some neurodegenerative diseases.

- **MICROMET's blinatumomab –** Interim results presented at the European Hematology Association meeting showed that this monoclonal antibody met the primary endpoint – induction of complete remission (CR) or complete remission with only partial hematologic recovery (CR+) – in 9 of 12 patients with relapsed/refractory B-precursor acute lymphoblastic leukemia (ALL). The study also met the

secondary endpoint of becoming MRD-negative or molecular remission.

- **Multiple sclerosis (MS)** – A study published in the ***Archives of Neurology*** found that the yellow fever vaccine might be risky for MS patients.

- **OREXIGEN THERAPEUTICS' Contrave (naltrexone SR + bupropion SR)** – The company is giving up on this obesity drug. In February, the FDA told Orexigen that it would have to conduct a cardiac safety trial before approval, and the company's efforts to get the FDA to agree to a scaled-back study were unsuccessful.

- **PACIRA PHARMACEUTICALS' Exparel (bupivacaine extended-release liposome injection)** – The FDA asked the company for additional information about this long-acting, non-opioid pain drug. When the company submitted those data, the FDA ruled it a major amendment and extended the review process by three months. The new PDUFA date is October 28, 2011.

- **Percutaneous coronary intervention volume** is likely to remain flat to slightly down over the next 6 months, according to a ***CRTonline*** poll, with 43% of cardiologists saying volume would be flat, 31% saying it would decrease, and 26% saying it would increase.

- **PEREGRINE PHARMACEUTICALS' bavituximab** – In a 49-patient Phase II study, non-small cell lung cancer patients lived for an average of 12.4 months, or about two months longer than patients treated with standard therapies. Previously, the company said 42% of patients responded to the drug, and the median time to death or disease progression was 6.1 months.

- **PfēNEX** has formed a non-exclusive partnership with **SAFC**, a unit of biopharmaceutical contract manufacturing firm **Sigma-Aldrich**, under which Pfēnex will engineer production strains and processes for SAFC's contract manufacturing customers. The developed processes will ultimately be transferred to SAFC's recently expanded fermentation facility in Jerusalem, Israel, for cGMP production. The companies also plan to work together to combine Pfēnex's Reagent Proteins vaccine component products with SAFC's products.

- **PFIZER and ACURA PHARMACEUTICALS' Acurox – now Oxecta (oxycodone immediate-release)** – At press time, rumor had it, but there was no official announcement, that the FDA had approved this painkiller, though without the original niacin component. *Will there be much clinical interest in this drug without the niacin?*

- **PHILIPS HEALTHCARE** – The FDA issued a warning letter that Philips failed to resolve several procedural violations that were identified during an inspection in late 2010 at its plant in Highland Heights OH. The company produces CT and nuclear medicine scanners at the Ohio facility.

- **PURDUE PHARMA's OxyContin (oxycodone)** – ***The New York Times*** reported that drug abuse experts and law enforcement officials believe OxyContin abuse has declined since the introduction of the reformulation, but, instead, addicts are turning to other drugs, with demand particularly high for pure 30 mg oxycodone pills, for **Endo Pharmaceuticals**' Opana ER (extended-release oxymorphone), and for heroin.

- **SANOFI** will collaborate with **Audion Therapeutics** to develop therapies that could restore hearing loss.

- **SEATTLE GENETICS and ASTELLAS PHARMA/AGENSYS' ASG-22ME** – The companies are collaborating on this antibody to treat solid tumors. Astellas filed for FDA permission to start Phase I trials.

- **SERUM INSTITUTE OF INDIA's MenAfriVac** – A report in the ***New England Journal of Medicine*** found this vaccine to be better at protecting people from a strain of meningitis in sub-Saharan Africa than **GlaxoSmithKline**'s Mencevax ACWY.

- **SUNOVION PHARMACEUTICALS' ciclesonide**, a hydrofluoroalkane nasal spray licensed from **Nycomed**, was accepted by the FDA for review to treat allergic rhinitis in patients age ≥12.

- **TENGION** – The FDA gave orphan drug status to the company's tissue regeneration technology for bladder cancer, which currently is in a Phase I trial. The technology isn't being used to develop a new bladder but to make functional tissue that can form a conduit to divert urine from the ureter to a removable, disposable bag outside the body.

- **TEVA's** planned merger with **Cephalon** has been delayed because the Federal Trade Commission (FTC) made a second request for information. The companies remain optimistic that the deal will close in 3Q11.

- **THE TRIAD GROUP** – The FDA obtained a consent decree of condemnation, forfeiture, and permanent injunction against this company, its parent, **H&P Industries**, and three individuals, preventing the company from resuming the manufacture or distribution of drugs or devices until it establishes quality control and assurance procedures, and until the identity, purity, potency, and safety of its products are established by an independent good-manufacturing-practice expert.

- **VIROPHARMA's Cinryze (complement C1 esterase inhibitor)** – European regulators approved this drug to prevent and treat angioedema attacks in adults and adolescents, and the approval provides that properly trained patients can self-administer Cinryze.
- **ZIOPHARM ONCOLOGY's ZIN ATI-001** – The FDA gave the company the go-ahead for a Phase I trial of this melanoma drug.

NEWS IN BRIEF

Alzheimer's disease – diet can affect biomarker

A 49-patient, short-term, randomized study reported in the ***Archives of Neurology*** found that a low-fat diet led to improvements in a putative biomarker of Alzheimer's disease risk in patients with mild cognitive impairment, but it had the opposite effect in healthy older adults.

Mean levels of the 42-amino-acid form of amyloid-beta protein in cerebrospinal fluid (CSF AB42) *increased* in cognitively impaired patients after eating the low-fat diet for four weeks, while levels of this marker *declined* in healthy adults on the same diet. A high-fat diet produced no changes in CSF AB42 levels in patients with mild cognitive impairment, but normal controls had a substantial increase.

The researchers concluded, "Our study supports further investigation into the possibility that consumption of a diet high in saturated fat and simple carbohydrates may contribute to pathologic processes in the brain that increase the risk of Alzheimer's disease. Conversely, diets low in saturated fat and simple carbohydrates may offer protection against Alzheimer's disease and enhance brain health."

BIOGEN IDEC

- **Acquisitions** – The company is shopping for new compounds to treat multiple sclerosis and other neuro-degenerative diseases. A company official said Biogen might purchase companies outright or partner with them. Biogen is particularly interested in drugs that have completed Phase II testing.
- **Avonex (interferon beta-1a)** – European regulators approved an injectable pen version of this multiple sclerosis drug, and the company plans to make it available within a few weeks.

BOEHRINGER INGELHEIM

- **Pradaxa (dabigatran etexilate)** – A study published in ***Circulation*** found the 150 mg dose of this antithrombotic alternative to warfarin is cost-effective in high-risk atrial fibrillation patients but only if INR control with warfarin was not already good. Based on an estimated cost of $9/day for Pradaxa, warfarin was most cost-effective for patients at a moderate stroke risk ($CHADS_2$ of 1 or 2), but Pradaxa 150 mg was most cost-effective for patients with a $CHADS_2$ score of 2 if risk of hemorrhage was >6%/year, and Pradaxa 150 mg was most cost-effective for high-risk patients with a $CHADS_2$ score ≥3, regardless of hemorrhage rate.

  The researchers also found that Pradaxa 150 mg would always be more cost-effective than warfarin if its cost were ≤$1,800/year. They also suggested Pradaxa could be cost-effective in patients with a $CHADS_2$ score of 2 who have the CYP2C9 allele so they metabolize warfarin slower, provided the cost of the genetic test for CYP2C9 were <$200.
- **Spiriva (tiotropium)** – A meta-analysis of five trials with >6,500 patients, published in the ***British Medical Journal***, found this mist inhaler for chronic obstructive pulmonary disease (COPD), made in partnership with **Pfizer**, might raise the risk of early death. They found Spiriva users were 52% more likely to die than COPD patients who used the inhaler with placebo. Last year, an FDA review concluded that Spiriva didn't increase the risk of heart attack and stroke despite earlier studies that suggested a potential risk.

BRISTOL-MYERS SQUIBB's Nulojix (belatacept) – gains FDA approval

This selective T-cell costimulation blocker was approved by the FDA to prevent acute rejection in adult patients who have had a kidney transplant. The drug, which is administered in a 30-minute infusion, is approved for use with other immuno-suppressants, specifically basiliximab and mycophenolate mofetil, and corticosteroids.

Nulojix was given a boxed warning about an increased risk of post-transplant lymphoproliferative disorder (PTLD), a cancer where white blood cells grow out of control after an organ transplant, especially in patients who have never been exposed to the Epstein-Barr virus (EBV). The approval of belatacept came shortly after the company got a passing grade from the FDA on its corrective measures to resolve deficiencies that were noted last year at its Puerto Rico manufacturing plant.

Carbonic anhydrase – a potential new cancer target

In a study published in the ***Journal of Biological Chemistry***, researchers from the University of Florida found that whether a tumor grows or dies depends, to a degree, on the acidity (pH) of the environment in which it lives, and they reported that the enzyme carbonic anhydrase IX influences tumor biology by keeping the pH level low, so normal cells die but cancer cells thrive.

"We believe that carbonic anhydrase is a significant player in picking the specific pH at which the cells are happiest," said Susan Frost, PhD, a biochemist from Shands Cancer Center. The enzyme may serve as a new target for visualizing, diagnosing, and treating cancer, particularly breast cancer. Blocking carbonic anhydrase could help kill cancer cells by upsetting the pH balance, and it could boost the effectiveness of chemotherapy agents.

The researchers already have synthesized chemicals that can inhibit carbonic anhydrase, and they fitted those potential therapeutic compounds with a chemical structure that prevents them from getting inside cells, so that they will only affect the enzyme that works on the outside of the cell to alter acidity levels. In animal studies, the anti-enzyme greatly diminished tumor size and metastasis.

The goal now is a non-toxic IV therapy that alters the micro-environment to prevent or reverse tumor growth, and the researchers are collaborating with colleagues at Moffitt Cancer Center on this.

Cardiac resynchronization therapy (CRT) – 40% of patients might not benefit

A meta-analysis of five major trials (COMPANION, CARE-HR, REVERSE, MADIT-CRT, and RAFT) published in the ***Archives of Internal Medicine*** found that 4 of 10 patients who receive a CRT (biventricular pacing) might not benefit from the device – patients with a QRS duration of 120-149 msec. These findings suggest current guidelines for CRT might need to be revised.

The meta-analysis compared patients with QRS 120-149 vs. ≥150. The researchers found CRT is very beneficial in patients with QRS ≥150, with the risk of hospitalization and death reduced by 40% in these patients. On the other hand, the 40% of patients with a QRS <150 had "absolutely no benefit whatsoever in terms of mortality or other clinical events reduction with CRT."

In an accompanying editorial, Lynne Warner Stevenson, MD, of Brigham and Women's Hospital in Boston said the study showed "how we may be intoxicated by the enthusiastic presentations of new trials and how we may be rendered sober again by deeper analysis of the collective experience."

Cardiac stents

- **Biodegradable stent outlook –** A ***CRTonline*** survey found that 69% of responding cardiologists believe that a biodegradable polymer on a drug-eluting stent (DES) has an advantage over a durable polymer on a DES, with 18% disagreeing, and 12% saying they didn't know.
- **Fraud suit –** The Department of Justice (DOJ) has joined a whistleblower lawsuit, filed under seal in 2007 by Tennessee cardiologist Wood Deming, MD, alleging that cardiologist Eli Hage Korban, MD, engaged in fraudulent billing and overuse of medical services, violations of the Medicare False Claims Act. This is only the latest in a series of suits about stent over-utilization. The original suit includes allegations against the CEOs of two Tennessee hospitals – Jackson-Madison County General Hospital and Regional Hospital of Jackson – but the DOJ did not join in the action against those defendants.
- **Head-to-head trial – Johnson & Johnson**'s sirolimus-eluting **Cypher** and **Boston Scientific**'s paclitaxel-eluting **Taxus** had similar angiographic and clinical outcomes at five years in the 1,012-patient SIRTAX LATE trial.

5-Year Results of SIRTAX LATE Trial

Measurement	Cypher n=503	Taxus n=509	p-value (hazard ratio)
MACE (cardiac death, MI, and ischemia-driven TLR)	19.7%	21.4%	0.89
Cardiac death	5.8%	5.7%	Nss
MI	6.6%	6.9%	Nss
TLR	13.1%	15.1%	Nss
Annual TLR rate between 1 and 5 years	2.0%	1.4%	Nss

CT procedures – up 6% in 2010

A survey by IMV of 421 CT sites in the U.S. found that 81.9 million CT procedures were performed in 8,180 hospitals and non-hospital sites in 2010. Other findings included:

- Contrast agents were used in 55% of procedures, down from 67% in 2007.
- CT angiography procedures are performed by nearly 75% of CT sites.
- 46% of the CTs installed in 2010 were systems that had ≥64 slices.
- The average replacement cycle for a CT scanner is 8.3 years.

- Reducing the radiation dose to patients was rated a "very important" priority by 77% of respondents, but only 9% believed that concerns over radiation dose would slow the growth of CT procedures at their facilities.
- >25% of sites planning to buy a CT scanner between now and 2014 intend to get a >64-slice device.

Employer-sponsored insurance (ESI) – likely to decrease under Obamacare

A report from ***McKinsey Quarterly***, based on a survey of 1,300 employers, found the Patient Protection & Affordable Care Act (PPACA) led to 30% of employers definitely or probably ending employer-sponsored insurance after 2014. More than 50% of employers with a high awareness of health-care reform are likely to end employer-sponsored insurance, and 60% will plan to pursue alternatives to traditional employer-sponsored insurance.

The findings differed dramatically from the Congressional Budget Office's projections that ~7% of employees who are currently covered by employer-sponsored plans would have to switch to a plan offered in the health insurance exchanges.

Nancy-Ann DeParle, assistant to President Obama, called the McKinsey report an "outlier," writing in a White House blog, "We don't know what respondents were told or whether they had the chance to check with their colleagues or crunch the numbers for their business before responding…Unfortunately, the study misses some key points and doesn't provide the complete picture about how the PPACA will strengthen the healthcare system and make it easier for employers to offer high-quality coverage to their employees." She cited data from Rand that found employer-sponsored insurance would not change substantially.

In addition, Senate Finance Committee Chairman Max Baucus (D-MT) and nine House Democrats wrote letters to McKinsey asking the company to release the survey methodology, the specific questions, the funding source, etc.

5-alpha reductase inhibitors – FDA issues cancer warning

The FDA strengthened the warning label for 5-alpha reductase inhibitors – such as **GlaxoSmithKline's Avodart (dutasteride)** and **Jalyn (dutasteride + tamsulosin)** and **Merck's Proscar (finasteride)**, which treat benign prostate hyperplasia (BPH), and Merck's hair-loss treatment **Propecia (finasteride)** – after a review of two large studies (the Prostate Cancer Prevention Trial and the REDUCE trial) indicated that men taking the drugs have a low but increased risk of developing high-grade prostate cancer.

Gastroesophageal reflux disease (GERD) – cancer risk lower than previously thought

A study reported in the ***Journal of the National Cancer Institute*** suggests that the risk of developing Barrett esophagus (defined by changes in the lining of the esophagus) is lower than doctors had thought, and GERD patients may require less intensive screening. Researchers studied 8,522 adults over a 7-year period in a Northern Ireland registry and found that only 0.13% of people with Barrett esophagus will develop esophageal cancer (~1 in 770) and only 0.22% (~1 in 450) will develop either esophageal or gastric cancer or severe precancerous tissue changes. The researchers also found that esophageal cancer was more likely to develop in men than in women, in patients ages 60 to 70 years, and in patients of lower socioeconomic status.

JOHNSON & JOHNSON

- **Drug confusion** – The FDA issued an alert, warning doctors that they are confusing the company's antipsychotic **Risperdal (risperidone)** with **GlaxoSmithKline**'s drug for Parkinson's disease and restless leg syndrome, **Requip (ropinirole)**. The FDA identified 226 medication errors, including five hospitalizations, caused by doctors confusing these two medications. The Agency cited several reasons for doctors confusing the two drugs: generic name similarity, label and packaging similarities, overlapping product characteristics (dosage forms, dosing intervals, drug strength), and illegible prescriptions.
- **Hip approval** – **Pinnacle CoMplete Acetabular Hip System**, the first ceramic-on-metal implant for total hip replacement. The femoral head is ceramic, and the acetabular (socket) component is a metal alloy. J&J agreed to conduct a postmarketing study to monitor patients for adverse events and metal ion concentrations in their blood.
- **Stent exit** – The company is getting out of the cardiac stent business, terminating development of its next-generation **Nevo DES** and discontinuing the entire **Cypher** franchise around end of 2011. *Why is J&J shuttering Cypher instead of selling it?*

MERCK

- **New labels** – The company redesigned the labels for 16 drugs, including diabetes drug **Januvia (sitagliptin)** and allergy drug **Singulair (montelukast)**, to help prevent

dispensing errors. The new labels use a standardized format to improve readability and dosage differentiation.

- **Partnership –** The company is teaming up with **Hanwha Chemical**, a South Korean company, on Hanwha's generic version of **Amgen's Enbrel (etanercept)**, which currently is in a Phase III trial. Merck plans to handle clinical development and manufacturing in all countries except South Korea and Turkey.
- **Vaccine trial stopped –** Merck and Intercell ended a trial of a V710, a *Staphylococcus aureus* vaccine, for futility, saying that the vaccine was not working and that mortality and multiple organ failure was higher in vaccine-treated patients.

NOVARTIS

- **Bexsero**, a vaccine for bacterial meningitis, successfully protected toddlers receiving three doses against meningococcal serogroup B when later given extra doses, reducing their risk of contracting bacterial meningitis. Novartis is working with the FDA to design a U.S.-specific Phase III study.
- **Lucentis (ranibizumab) –** European regulators approved this macular degeneration drug, made in partnership with **Roche/Genentech**, for a new indication: macular edema secondary to retinal vein occlusion. Lucentis already had this indication in the U.S.
- **Pasireotide (SOM-230) –** A 6-month, 162-patient, Phase III trial presented at the Endocrine Society meeting found that this injectable somatostatin analogue reduced elevated cortisol levels ~50% in patients with Cushing's disease. This could become the first non-surgical/radiation therapy for this disease.

NOVO NORDISK's Victoza (liraglutide) – thyroid cancer and pancreatitis risk

Saying that some primary care providers were not fully aware of the serious risks associated with this Type 2 diabetes drug – risks which are outlined in Victoza's risk evaluation and mitigation strategy (REMS) – the FDA issued a warning to remind doctors that Victoza carries dose-dependent and treatment-duration-dependent risk of both thyroid cancer, including medullary thyroid carcinoma, and pancreatitis. The FDA ordered the company to issue a Dear Healthcare Professional letter.

PFIZER

- **Chantix (varenicline) –** After reviewing a randomized, double-blind, placebo-controlled trial of 700 smokers, the FDA decided to change the label for this smoking cessation drug to warn about a "small" increased risk of cardiovascular adverse events (non-fatal MI, angina, revascularization, etc.) in patients who have cardiovascular disease. The FDA is continuing to evaluate the cardiovascular safety of Chantix and is requiring Pfizer to conduct a large meta-analysis of randomized, placebo-controlled trials.
- **Detrol (tolterodine) –** Pfizer is conducting the first FDA-approved, all-electronic drug trial with this overactive bladder drug. Patients participate from home via computer or smartphone.
- **Generics –** Pfizer is partnering with China's **Zhejiang Hisun Pharmaceutical Co.** to produce low-cost generics, focusing on branded generics, for the Chinese market.
- **Inotuzumab ozogamicin –** Updated data from an ongoing, 59-patient Phase II trial (Study 2001) in B-cell non-Hodgkin's lymphoma (NHL) on this antibody-drug conjugate – an anti-CD22 monoclonal antibody linked to calicheamicin (a cytotoxic) – were presented at the International Conference on Malignant Lymphoma in Lugano, Switzerland. The study evaluated 59 patients with indolent NHL refractory to rituximab, rituximab + chemotherapy, or radioimmunotherapy, and found encouraging response rates and a "generally favorable" toxicity. A multicenter, open-label, randomized Phase III trial is ongoing.

Inotuzumab Ozogamicin Phase II Results

Measurement	Inotuzumab ozogamicin
ORR overall	55%
ORR in patients with follicular lymphoma	62%
CR in follicular lymphoma patients	10 patients
PFS in follicular lymphoma patients	50%
Adverse events	
Thrombocytopenia	67%
Neutropenia	52%
Aspartate aminotransferase elevation	47%
Nausea	47%
Fatigue	43%
Leukopenia	34%
Lymphopenia	34%

- **Center for Therapeutic Innovation –** Pfizer partnered with leading Boston-area hospitals, medical schools, and universities to bridge the gap between basic science discoveries and drug testing of those advances. Pfizer plans to invest $100 million over five years and establish the Center for Therapeutic Innovation in the Longwood Medical Area. Pfizer scientists will work in teams with academic researchers, jointly planning and pursuing ideas generated by doctors and academic scientists in the Boston area. Pfizer will decide whether to take over a project only after it completes Phase I testing.

Physician-owned distributorships (PODs) – under scrutiny

Five U.S. senators asked the Inspector General of the Department of Health and Human Services (HHS) to investigate PODs whether they are legal if the surgeon owners profit from the medical devices they use on patients and to issue an initial report by August 12, 2011. The questions are whether they violate the anti-kickback statute and other federal fraud and abuse laws and whether they encourage unnecessary procedures. PODs have become popular in the spine market, springing up in 20 states and accounting for up to 15% of the spine hardware market.

QRXPHARMA's MoxDuo IR (Q8003 IR) – positive Phase III results

The company announced successful completion of Study 022 – a double-blind, randomized, fixed-dose, Phase III trial in 375 patients post-bunionectomy – of the tolerability and safety of MoxDuo vs. equi-analgesic doses of either morphine or oxycodone alone. The primary endpoint of respiratory depression (oxygen desaturation) was less severe and of shorter duration with MoxDuo (12 mg/8 mg) vs. morphine (24 mg) or oxycodone (16 mg) alone. Moderate-to-severe vomiting was also less frequent with MoxDuo vs. oxycodone. QRxPharma plans to submit MoxDuo to the FDA in 2011 and to European regulators in 1H12.

SALIX PHARMACEUTICALS' Xifaxan (rifaximin) – interesting results in *C. diff*

According to research presented at the European Congress of Clinical Microbiology and Infectious Diseases, a rifaximin "chaser" decreases recurrent diarrhea in patients with *C. difficile* (*C. diff*). The results came from a double-blind, placebo-controlled, 68-patient pilot study comparing rifaximin 400 mg TID given immediately after finishing conventional antibiotic therapy vs. oral vancomycin or metronidazole for 20 days vs. placebo. The researchers reported that 21% of the rifaximin patients had recurrent diarrhea vs. 49% of placebo patients (p=0.010).

Simvastatin – warning about high doses

After data from a 7-year study confirmed there is a greater risk of myopathy with high-dose (80 mg) simvastatin [**Merck**'s Zocor and generics], the FDA warned doctors not to use that dose unless patients already have been on the statin for more than a year without muscle pain. The FDA also changed the cholesterol-lowering drug's label to warn about an increased risk of muscle injury or myopathy with 80 mg, particularly during the first 12 months of use.

The FDA also issued a safety alert for Merck's simvastatin-containing medicines – Merck's Vytorin (simvastatin + ezetimibe) and Abbott's Simcor (simvastatin + niacin ER).

TAKEDA's Actos (pioglitazone) – bladder cancer risk

Two European countries banned use of Actos, citing the risk of bladder cancer. Then, two days later, the FDA announced that the Actos label was being revised to highlight the bladder cancer risk after its review of interim data from an ongoing study found that patients taking Actos for >1 year might have an increased risk of bladder cancer.

TEVA

- **Lipegfilgrastim** – The company announced that this long-acting granulocyte colony-stimulating factor (G-CSF) performed better than **Amgen**'s **Neulasta (pegfilgrastim)** in treating neutropenia in a Phase III trial in >200 breast cancer patients.
- **Teriflunomide** – Adding a 7 mg/day dose of this oral multiple sclerosis drug to Teva's injectable multiple sclerosis drug **Copaxone (glatiramer acetate)** decreased MRI lesions by nearly two-thirds vs. Copaxone alone (p=0.03), according to a study presented at a meeting of the Consortium of Multiple Sclerosis Centers.

  However, the relapse rate was reduced 38%, but that was not a statistically significant reduction (p=0.22). In addition, a higher dose (14 mg/day) had a smaller effect on MRI lesion burden than the lower dose, but the annualized relapse rate was slightly higher than in the Copaxone-only patients. *So, the results raise a lot of questions.*

  The Phase III TERACLES trial of teriflunomide + Copaxone + interferon started earlier this year, with results expected in 2014.

48-Week Results of Trial of Copaxone + Teriflunomide

Measurement	Placebo	Copaxone +	
		Teriflunomide 7 mg/day	Teriflunomide 14 mg/day
MRI lesion count	0.333	0.120 (p=0.31)	0.178 (Nss, p=0.193)
Annualized relapse rate	0.420	0.262 (Nss, p=0.217)	0.497 (Nss, p=0.574)

THORATEC's HeartMate II – more complications than older model

Data from Henry Ford Hospital (a single-center, 64-patient study), presented at the American Society of Artificial Internal

Organs (ASAIO) symposium, indicated that the HeartMate II continuous-flow left ventricular assist device (LVAD) increased both gastrointestinal bleeds and strokes vs. the earlier model, HeartMate XVE. An analysis of the single-center experience found:

- 21.9% of HeartMate II patients had a GI bleed. The only independent predictor of this was a prior history of a GI bleed. GI bleeding did not have a significant impact on survival.
- 7.5% of HeartMate II patients had a major adverse neurological event (4 intracranial hemorrhages and 1 thromboembolic stroke). These tended to be older patients, with more chronic renal insufficiency and higher INRs. A major neurological event reduced survival.

VALEANT PHARMACEUTICALS' Potiga (ezogabine) – gets FDA approval

This neuronal potassium channel opener was approved by the FDA for use as an add-on medication to treat partial seizures associated with epilepsy in adults. The company was required to produce a medication guide to be distributed each time a patient fills a prescription. In addition, the FDA mandated a REMS for Potiga to inform healthcare professionals about the risk of urinary retention, which occurred in ~2% of patients in clinical trials.

Potiga also was classified as a controlled substance subject to scheduling by the Drug Enforcement Administration (DEA). Valeant cannot launch Potiga until the DEA completes the scheduling process, which could take up to six months.

VERTEX PHARMACEUTICALS

- **VX-770** and **VX-809** – The company reported initial results from a Phase II study indicating the combination of these two cystic fibrosis drugs is safe, with no serious treatment-related side effects. The trial also met the efficacy endpoint, significantly reducing sweat chloride (by 13.2 mmol) through 21 days.
- **Hepatitis C** – Vertex licensed two oral Hepatitis C drugs from **Alios BioPharma** and plans to start Phase I testing later this year.

REGULATORY NEWS

CMS: No national decision on anemia drugs

CMS decided not to issue a national coverage determination on anemia drugs – **Amgen's Aranesp (darbepoetin)** and **Epogen (epoetin)** and **J&J's Procrit (epoetin)** – saying simply, "Given the totality of the currently available evidence, CMS will not issue a national coverage determination at this time."

CMS proposes physician rating rules

The Centers for Medicare and Medicaid Services (CMS) is proposing to use its claims data to compare physician performance. CMS is accepting comments on the proposed rule until the beginning of August 2011. Under the 90-page proposal, certain organizations – e.g., quality-ranking organizations – would get access (for a fee) to the CMS claims database starting in 2012, and they could combine that with claims data from private insurers to determine how physicians, hospitals, and other providers are performing.

That means information about how individual doctors in a given location (region, city, state, etc.) are performing on specific quality and patient care measures will soon be public. However, before the data can be made public, individual physicians who are singled out in the report must be given a chance to review the data and to correct any errors.

Medicaid to stop paying for never events

As of July 1, 2011, CMS will no longer reimburse states for any amounts expended for providing medical assistance for provider-preventable events, including healthcare-acquired conditions.

CMS urged to cut reimbursement for imaging services

In a report to Congress, the Medicare Payment Advisory Commission (MedPAC) recommended reducing reimbursement, bundling payments, and requiring prior authorization for imaging services. The four recommendations were:

- Accelerate and expand efforts to package discrete services in the physician fee schedule into larger units for payment.
- Apply a multiple procedure payment reduction to the professional component of diagnostic imaging services provided by the same doctor in the same session.
- Reduce the physician work component of imaging and other diagnostic tests that are ordered and performed by the same doctor.
- Establish a prior authorization program for doctors who order substantially more advanced diagnostic imaging services than their peers.

The report noted that physician investment in imaging equipment contributed to the rapid growth of testing and resulted in a high level of utilization that "likely includes unnecessary services."

FDA accused of approving orphan drugs on poor-quality data

An analysis in the ***Journal of the American Medical Association*** claimed the FDA is approving orphan drugs for rare cancers based on low-quality clinical tests with questionable scientific validity. The investigators reviewed FDA data from 2004 to 2010 and found the clinical testing quality of 15 approved orphan drugs was markedly lower than the testing quality of 12 approved non-orphan drugs. They said the orphan drug trials enrolled fewer patients, were less likely to be randomized, and were more likely to have adverse reactions than trials of non-orphan drugs.

FDA gives more power to Office of Compliance

The FDA's Center for Drug Evaluation and Research (CDER) elevated the Office of Compliance, making it a Super Office, on a par with the Office of New Drugs (OND), Office of Surveillance and Epidemiology (OSE), etc. Among the areas that Compliance regulates are human subject protection, adverse event and drug quality reporting, REMS, and drug labeling. The acting director of the new Compliance Super Office is Deborah Autor.

FDA explains 510(k) rejections

The FDA said 80% of medical devices submitted for 510(k) clearance did not show they were "substantially equivalent" to a predicate device and were rejected because of inadequate performance data.

FDA pleased with first year of *Bad Ad* program

On May 11, 2010, FDA's Center for Drug Evaluation and Research (CDER) launched the ***Bad Ad*** outreach program aimed at encouraging healthcare professionals to recognize and report suspected untruthful or misleading drug promotion. During the first year, the FDA sent letters to doctors, created an information video and a Bad Ad brochure, staffed exhibits at 15 medical conferences, and hosted a webinar.

The efforts led to 328 reports of potentially untruthful or misleading promotion (up from an average of 104 in prior years). The FDA said the number and diversity of the reports indicate that the program was successful in raising awareness of untruthful and misleading promotion. Only 4% of the reports were submitted anonymously.

- Of the 188 healthcare professional reports, 87 were identified for a comprehensive review.
- Of the 116 reports submitted by consumers, 24 were identified for a comprehensive review.
- Of the 24 reports submitted by industry, 14 were identified for a comprehensive review.

The FDA said many of the other reports were useful as well, helping to focus FDA's surveillance efforts in other ways or getting referred to other FDA Centers (e.g., the Center for Food or the Center for Devices and Radiological Health).

Going forward, the FDA plans to expand its Bad Ad efforts to include development of a web-based continuing education program, additional efforts focused on students and early career healthcare professionals, and collaborations with medical, pharmacy, and nursing schools to enhance student education.

Among the enforcement actions that came about because of the Bad Ad program were:

- **Hill Dermaceuticals' Derma-Smoothe** – warning letter in December 2010 after a complaint about a website promotion.
- **Forest Laboratories/Cypress Bioscience's Savella (milnacipran)** – notice of violation in April 2011 after a report by a physician about oral promotional statements.
- **Shire's Vyvanse (lisdexamfetamine)** – warning letter issued in May 2011 after a nurse reported a promotional piece was misleading because it was designed to hide the important risk information from plain view.
- **Three Rivers Pharmaceuticals' Infergen (interferon alfacon-1)** – warning letter in March 2011 after a pharmacist complaint about a direct mail piece that overstated the effectiveness of a product.
- **Warner Chilcott's Atelvia (risedronate delayed-release)** – warning letter issued in May 2011 for video footage of a violative product detail that occurred in a physician's office and was posted to YouTube.

FDA roadmap for nanotechnology regulation

The FDA released draft guidance to provide industry with more certainty about the use of nanotechnology. The guidance outlines the Agency's view on whether regulated products contain nanomaterials or involve the application of nanotechnology. The FDA specifically identified certain characteristics – such as the size of nanomaterials used and the exhibited properties of those materials – that may be considered when attempting to identify applications of nanotechnology in regulated products.

FDA Commissioner Margaret Hamburg, MD, said, "With this guidance, we are not announcing a regulatory definition of

nanotechnology. However, as a first step, we want to narrow the discussion to these points and work with industry to determine if this focus is an appropriate starting place."

For products subject to premarket review, the FDA intends to apply the draft guidance, when finalized, to better understand the properties and behavior of engineered nanomaterials. For products not subject to premarket review, the FDA will urge manufacturers to consult with the Agency early in the product development process so questions related to the regulatory status, safety, effectiveness, or public health impact of these products can be adequately addressed.

FDA warns pending bill would harm consumers

An amendment approved by the House Appropriations Committee would require the FDA to wait until people are harmed by unsafe drugs or food before taking action, the FDA said, adding, "FDA must sometimes act when there are credible risks, but before the weight of scientific evidence has been established."

Supreme Court rules: Pharma 1, Universities 0

By a vote of 7-2, the U.S. Supreme Court upheld a lower court decision in favor of **Roche** in a patent case, effectively limiting the rights of research universities to discoveries made by their researchers. The case involved a scientist working at Stanford University who transferred the rights to some of his discoveries to a company (**Cetus**) from which Roche later bought the rights to certain technology. The court said the transfer made the company a co-owner of three disputed patents.

Stanford had argued that the transfer was barred under the 1980 Bayh-Dole Act, which allocates patent rights among government, investors, and institutions that receive federal money. However, Chief Justice John Roberts said this law didn't displace the longstanding principle that inventors have first claim to their discoveries.

When the researcher started work at Stanford as a fellow in 1988, he signed an agreement saying he would assign his patent rights to the university. The next year the researcher began making visits to Cetus, which was collaborating with Stanford on some research. The researcher signed an agreement with Cetus, giving that company the rights to inventions stemming from his work there. Stanford argued that, because the underlying research was funded in part by the federal government, the Bayh-Dole Act barred the researcher from assigning his rights to Cetus.

Yet, the Supreme Court left open a way for universities to prevent a similar situation in the future: change the language in their agreements with researchers.

The case is Board of Trustees of the Leland Stanford Junior University v. Roche Molecular Systems, 09-1159.

U.K. pharmas oppose off-label prescribing

The Association of the British Pharmaceutical Industry has come out against a General Medical Council proposal that would allow clinicians to prescribe drugs for off-label use. The council said off-label prescribing "does not interfere with (doctors') ethical considerations," but the trade group contends that it threatens patient safety and drug development.

European regulatory news

- **AFSSAPS**, the agency in charge of overseeing healthcare products in France, is seeking comments from industry and healthcare experts on the current medical device maintenance regulations to determine if the rules need to be revised. The agency set a July 22, 2011, deadline for comments.
- **JOHNSON & JOHNSON's Animas Vibe** – J&J plans to market this insulin pump, which includes **DexCom**'s continuous glucose monitor **G4 Sensor**, in several European countries, including the U.K. and Germany.
- **The U.K.'s National Institute for Health and Clinical Excellence (NICE)** issued draft guidance saying **GlaxoSmithKline** and **Valeant**'s **Trobalt** (retigabine) could be paid for as an add-on epilepsy treatment option if other drugs do not work or have unmanageable side effects.

FDA approvals/clearances

- **ENDOLOGIX's AFXT**, an endovascular abdominal aortic aneurysm repair system.
- **KONICA MINOLTA MEDICAL IMAGING's Regius Sigma tabletop CR reader**, designed for use in low-volume clinics, received 510(k) clearance.
- **MAZOR ROBOTICS' Renaissance** – This next-generation spinal surgical robot was cleared.
- **RAPID PATHOGEN SCREENING's RPS Adeno Detector Plus** – This quick, point-of-care conjunctivitis test received 510(k) clearance. The company is expecting to get a CLIA waiver.
- **ROCHE/VENTANA's Inform Dual ISH**, a genetic test to help determine whether breast cancer patients are HER2-positive and candidates for Roche/Genentech's Herceptin (trastuzumab).

- **SIEMENS HEALTHCARE**
  - **Biograph mMR** – This scanner that allows PET and MRI scanning simultaneously was approved by the FDA. Earlier this month, it was cleared by European regulators.
  - **Luminos Agile Fluoroscopy/Radiography system** – This patient-side controlled system with flat-panel detector technology, a height-adjustable table, and dual-use capability for fluoroscopy and radiography received 510(k) clearance.
- **SMART Leish PCR assay**, which uses polymerase chain reaction to help detect cutaneous leishmaniasis – which was developed by Cepheid USA and the Army Medical Research and Materiel Command.
- **SQI DIAGNOSTICS' automated technology** and assays for celiac disease testing. The tests already were approved in Canada.

FDA recalls

There were quite a few recalls of note not already mentioned during this two-week period, including:

- **AMERICAN REGENT**
  - **Concentrated sodium chloride injection** – because some of the vials contain visible particulates.
  - **Methyldopate HCl injection**, a hypertension medication – one lot because some vials have translucent glass particulates that can disrupt blood flow within small blood vessels in the lung or cause localized inflammation or granulomas.
- **BOSTON SCIENTIFIC**
  - **iCross and Atlantis SR Pro 2 Coronary Imaging Catheters** – due to the possibility of the catheter tip breaking inside the patient and causing an embolization.
  - **Innova**, an over-the-wire, self-expanding superficial femoral artery (SFA) stent system – A Class I recall because of complaints of no deployment and partial deployment, which can result in vessel wall injury, increase procedure time, and/or require emergency surgery to remove the stent.
  - **Latitude Patient Management System** – because data in certain printed reports obtained from the device might not be accurate or might have missing data.
- **BRISTOL-MYERS SQUIBB's Plavix (clopidogrel)** – due to chemical contamination with 2,4,6-tribromoanisole (TBA).
- **CARACO PHARMACEUTICAL LABORATORIES' alendronate** – due to labeling error about dosage.
- **CELGENE's Innohep (tinzaparin sodium injection)** – due to particulate matter (glass, metal, wood).
- **JOHNSON & JOHNSON's Topamax (topiramate)** due to chemical contamination.
- **ORIDION MEDICAL and PHILIPS HEALTHCARE's Microstream CO_2 Filterline** – a device used by emergency medical services, hospitals, and other healthcare providers to measure exhaled carbon dioxide (CO_2) during ventilation of newborn and infant patients.
- **RANBAXY's Calan SR (verapamil hydrochloride)** – because the Pfizer manufacturing site in Puerto Rico is currently not an approved manufacturing site.
- **ROCHE's Xeloda (capecitabine)** – due to chemical contamination with low levels of naphthalene and/or 1,4 dichlorobenzene causing an off odor.
- **TEVA**
  - **amoxicillin** – due to lack of product stability.
  - **azithromycin** – due to manufacturing tests that were not performed to specifications.
  - **clonazepam** – because tablets may not conform to weight specifications.
  - **Enjuvia (synthetic conjugated estrogen)** – due to subpotent test results.
  - **glyburide and metformin** – due to manufacturing tests that were not performed to specifications.
- **TERUMO's Coronary Ostia Cannula** – This device used to deliver cardioplegia solution to coronary arteries during cardiopulmonary bypass was recalled due to foreign fragments of adhesive and plastic in the cannula tip that might embolize and cause arterial injury, hemorrhage, etc., requiring unplanned surgery. Terumo decided to pull the product from the market and discontinue further supply.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	June	
June 20	**Salix Pharmaceuticals' Xifaxan** (rifaximin) for non-constipation IBS	Company to meet with FDA on complete response letter
June 21	**Novartis' Ilaris** (canakinumab) for the treatment of gouty arthritis attacks	FDA's Arthritis Advisory Committee
June 23	**Shire's Firazyr** (icatibant injection) for hereditary angioedema	FDA's Pulmonary-Allergy Drugs Advisory Committee
June 23	**Pfizer/King Pharmaceuticals/Pain Therapeutics' Remoxy** (tamper-resistant oxycodone CR) for pain	PDUFA date
June 23-24	**HCV drug development**	Workshop on Clinical Pharmacology of Hepatitis Therapy, Boston
June 28-29	**Roche/Genentech's Avastin** (bevacizumab), hearing on appeal of FDA's decision to withdraw the indication for metastatic breast cancer	FDA's Oncologic Drugs Advisory Committee (ODAC)
June 29	**Cellular and gene therapy products** for retinal disorders	FDA's Cellular Tissue and Gene Therapies Advisory Committee
	July	
July 11	**Novartis' Arcapta Neohaler** (indacaterol) long-acting beta agonist (LABA) for COPD	PDUFA date
July 14	**Seattle Genetics' brentuximab vedotin** to treat both relapse/refractory Hodgkin's lymphoma and relapsed/refractory systemic anaplastic large cell lymphoma	FDA's Oncologic Drugs Advisory Committee
July 19	**Bristol-Myers Squibb and AstraZeneca's dapagliflozin,** the first SGLT2 inhibitor for Type 2 diabetes	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
July 20	**Edwards Lifesciences' Sapien** percutaneous aortic valve	FDA's Circulatory System Advisory Committee
July 20	**AstraZeneca's Brilinta** (ticagrelor), an anticoagulant	PDUFA date
	August	
August 12	**Physician-owned distributorships (PODs)**	Inspector General initial report due to Senate Finance Committee
August 20	**Regeneron's aflibercept** (VEGF Trap-Eye) for wet AMD	PDUFA date
August 25	**Shire's Firazyr** (icatibant injection) for hereditary angioedema	PDUFA date
August 30	**Seattle Genetics and Takeda's brentuximab vedotin** for two orphan indications – refractory Hodgkin's lymphoma and anaplastic large cell lymphoma (ALCL)	PDUFA date
	Other 2011 meetings/events	
Summer	Report on **FDA 510(k) reform**	Institute of Medicine
2H11	**Abbott's RX Acculink** carotid stent	FDA final decision expected
4Q11	**Ophthotech's ARC-1905** primary endpoint results in Phase I trial in dry AMD	Company announcement or medical conference presentation
4Q11	**Roche/Genentech's Lucentis** (ranibizumab) – Phase III HARBOR trial one-year data on the 2 mg dose in wet AMD	Company announcement or medical conference presentation
October 28	**Pacira Pharmaceuticals' Exparel** (bupivacaine extended-release liposome injection), a painkiller	PDUFA date
December	**Allergan's brimonidine tartrate intravitreal implant** – Phase II trial in dry AMD to complete	Company announcement or medical conference presentation
December 8	**Antares Pharma's Anturol Gel** (oxybutinin gel), a treatment for overactive bladder	PDUFA date
	2012 meetings/events	
February 2012	**Alcon's tandospirone** for dry AMD – Phase III final data expected	Company announcement or medical conference presentation