TRENDS-in-MEDICINE

May 29, 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

- **ACTELION's CRTH2 antagonist** – The company announced positive results from a Phase II study in seasonal allergic rhinitis due to mountain cedar pollen. The prospective, randomized, parallel-group, double-blind, placebo-controlled, multiple-dose, 579-patient trial met its primary endpoint at 2 weeks, significantly decreasing the Daytime Nasal Symptom Score, with no serious adverse events reported.
- **AMPIO PHARMACEUTICALS' Zertane (tramadol hydrochloride)** – The company said this drug to treat premature ejaculation showed statistically significant results in a Phase III European trial, and Ampio plans to use those data to file for European regulatory approval.
- **AUROBINDO PHARMA** – The FDA gave the company 15 working days to submit a plan for correcting antibiotic labeling and packaging problems at its Hyderabad, India, plant. The FDA previously issued an import alert on cephalosporins produced at the plant. The company said it has asked for a date to meet with the FDA.
- **BAYER aspirin** – Bayer introduced a reformulated aspirin that works twice as fast as its regular aspirin. On average, the company claims the 500 mg dose starts working in 16 minutes and brings "meaningful" pain relief in 49 minutes (vs. 100 minutes for regular Bayer aspirin).
- **BECKMAN COULTER's Synchron LX Clinical Systems Ion Selective Electrolyte (ISE) Flow Cell** – The FDA notified laboratory managers of a Class I recall of these clinical chemistry analyzers due to incorrect electrolyte results that can occur due to silver iodide build-up on parts, microbial contamination, and maintenance issues. The root cause has not been definitively identified, but it may be a maintenance-related issue.
- **BRISTOL-MYERS SQUIBB and PFIZER's Eliquis (apixaban)**, an oral direct Factor Xa inhibitor, was approved by European regulators for the prevention of venous thrombo-embolic events (VTEs) in adults who have undergone elective hip or knee replacement surgery.
- **DIGISONICS' DigiView software** – Releases 3.6.4.4, 3.6.4.6, and 3.6.5.2 were recalled because of a failure of the software to update some measurements when tracings or points are amended after measurement calculations have been performed.
- **HISAMITSU PHARMACEUTICAL/NOVEN PHARMACEUTICALS' Pexeva (paroxetine mesylate)** – The FDA ordered the company to cease dissemination of promotional materials for this antidepressant that the Agency found omits and minimizes important risk information.

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- **HUMAN GENOME SCIENCES and GLAXOSMITHKLINE's Benlysta (belimumab)** – The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion on this lupus drug.

- **JOHNSON & JOHNSON** is buying over-the-counter drugs – including Rinza and Doktor Mom, the No. 1 and No. 2 cough/cold medication brands in Russia – from **JB Chemicals & Pharmaceuticals**. J&J plans to market the products in Russia and other countries.

- **LILLY's Xigris (drotrecogin alfa)** – Lilly plans to work with two private investors (Care Capital and NovaQuest Capital) to create a privately held biotechnology company, **BioCritica**, to sell this sepsis drug and perhaps to develop other drugs. BioCritica also will have an option to acquire development and commercialization rights to Xigris outside the U.S.

- **MAP PHARMACEUTICALS' Levadex (inhaled dihydroergotamine)** – The company submitted a 505(b)(2) application, seeking FDA approval of Levadex to treat acute migraine headaches.

- **NEUROSEARCH's tesofensine** – After meeting with FDA and European regulators to work out a clinical development plan, the company said it will not invest any more of its own money in this obesity drug. Instead, it will look for a partner.

- **OPTIMER PHARMACEUTICALS' Dificid (fidaxomicin)**, a macrolide antibacterial, was approved by the FDA for the treatment of *Clostridium difficile*-associated diarrhea (CDAD). It is taken BID for 10 days, but the FDA is advising doctors to use it only to treat infections that are proven or strongly suspected to be caused by *C. diff* to maintain the effectiveness and reduce the development of drug-resistant bacteria.

- **PAR PHARMACEUTICAL** is buying privately held Indian pharma **Edict Pharmaceuticals**, which makes solid, oral-dose generic drugs and currently has seven abbreviated new drug applications (ANDAs) under FDA review and another 14 products in development.

- **PHARMAXIS' Bronchitol (inhaled mannitol)** – European regulators warned the company it is unlikely to get approval for this cystic fibrosis treatment. The regulators reportedly are concerned with the company's lack of an explanation for efficacy in children and adults but not in adolescents. *However, **Trends-in-Medicine** reported in October 2010 that Bronchitol missed the primary endpoint in a Phase III trial, so it is puzzling why the EU rejection should be a shock.*

- **Polypill** – A study published in ***PLoS One*** found that a polypill – 75 mg aspirin + 75 mg lisinopril (an ACE inhibitor for hypertension) + 12.5 mg hydrochlorothiazide (a diuretic) + 20 simvastatin (a statin) – significantly reduced systolic blood pressure and LDL but caused more side effects than placebo. The researchers concluded that the benefits may outweigh the risks, especially for high-risk patients.

- **RADIUS HEALTH's BA-058** – Radius negotiated a deal with **Nordic Bioscience**, a Danish contract research organization, to manage its Phase III clinical trials of this injectable osteoporosis treatment in Europe, South America, and Hong Kong.

- **SERVIER's terutroban** – A study published in ***The Lancet*** found this antiplatelet agent failed to prevent a second stroke in someone who already had a stroke. Preclinical research had been positive, but the study had to be stopped early for futility.

- **SSRI antidepressants** – An article in the ***Proceedings of the National Academy of Sciences*** reported that the antagonist effect of non-steroidal anti-inflammatory drugs (NSAIDs) on SSRIs is specific for SSRIs, not all classes of antidepressants. The researchers also noted there is no evidence that NSAIDs alone have any treatment effect on depressive-like states.

- **VALEANT PHARMACEUTICALS INTERNATIONAL** is acquiring Lithuanian specialty pharmaceutical company **AB Sanitas**, with the deal expected to close in 4Q11.

- **WATSON PHARMACEUTICALS** is acquiring **Specifar Pharmaceuticals**, a Greek generic pharma.

NEWS IN BRIEF

ABBOTT's Niaspan (extended-release niacin) – outlook dim as trial found raising HDL doesn't improve CV outcomes

The National Heart, Lung, and Blood Institute (NHLBI), a division of the National Institutes of Health (NIH), stopped the 3,404-patient AIM-HIGH trial 18 months ahead of schedule because the Data and Safety Monitoring Board (DSMB) declared the trial futile. The DSMB found that adding high-dose Niaspan to a statin in people with heart and vascular disease did not reduce the risk of cardiovascular (CV) events (e.g., MI and stroke).

Patients in AIM-HIGH had well-controlled LDL but a history of CV disease, low HDL, and high triglycerides. One aim of AIM-HIGH was to prove that raising HDL is beneficial. Since

low HDL is a risk factor for CV disease, it was widely thought – but never really proven – that raising HDL would be beneficial. With 32 months of follow-up the niacin/statin therapy did increase HDL and lower triglycerides, but there was no corresponding decline in fatal or non-fatal MIs, strokes, hospitalizations for acute coronary syndrome, or revascularizations. Obviously, AIM-HIGH did not provide the proof that raising HDL is beneficial.

The DSMB also noted a small and unexplained increase in ischemic strokes in the high-dose Niaspan group (1.6% vs. 0.7% for control), giving the NHLBI another reason to stop the trial early. Almost a third of the strokes in the Niaspan patients occurred after they stopped the drug, and prior trials did not identify any stroke risk with Niaspan or niacin. So there is still a possibility this is a statistical anomaly.

Abbott isn't giving up easily. The company said, "The AIM-HIGH study population does not represent all patient populations in whom the importance of treating low HDL and lowering triglycerides with Niaspan may be significant."

Alzheimer's disease – still no proof for prevention strategies

An article in the ***Alzheimer's Research Forum Newsletter*** reported on the debate over prevention of Alzheimer's disease. Last year a State-of-the-Science panel convened by NIH found insufficient evidence to recommend any health intervention to prevent Alzheimer's disease.

Many experts have argued this sent the wrong message to the public, especially about the value of lifestyle choices. A new article published in the ***Archives of Neurology*** again concluded there is not enough evidence to make definitive links between lifestyle choices or health conditions and the risk of Alzheimer's, but these researchers said there are some consistent, if weak, associations with diabetes, hyperlipidemia in midlife, and current tobacco use.

The ***Archives of Neurology*** authors also found an association with lower risk for healthy habits such as physical and cognitive exercise, low-to-moderate alcohol intake, folic acid intake, and a heart-healthy diet. However, the authors rated the quality of the evidence "low" for all of these. The bottom line: More studies are needed.

Congress and pharma

- **Drug-safety data** – The Senate Judiciary Committee approved the Sunshine in Litigation Act, which would require the release of drug-safety information used in pharmaceutical product liability cases. If enacted into law, the legislation would make it more difficult for judges to seal court records in these cases and make it easier to access information about defective and dangerous products.
- **Pharma mergers** – Sen. Herb Kohl (D-WI) wrote a letter to Federal Trade Commission chairman Jonathan Leibowitz warning that more pharma mergers could "exacerbate already critical drug shortages." He asked the FTC to be "cognizant of these shortages when applying antitrust law to the drug industry."

Congress – investigating drug pricing

- **Avanir Pharmaceuticals' Nuedexta (dextromethorphan hydrobromide and quinidine sulfate)** – Congressional Democrats also requested pricing information on this treatment for pseudobulbar affect. Nuedexta costs ~$600/month, but the two ingredients – quinidine and dextromethorphan – are cheap (~$20) generic drugs.
- **URL Pharma's Colcrys (colchicine)** – When the FDA barred generic colchicine products, a common gout treatment, from the market because they had not gone through the approval process, it left only Colcrys on the market. URL raised the price of its drug significantly. Now, four congressmen are looking into the price increase. They sent the company's CEO a letter demanding an explanation and setting a June 10 deadline for the response.

MEDTRONIC's Infuse (rhBMP-2) – linked to male sterility

A retrospective study by Stanford researchers published in ***The Spine Journal*** found this bone morphogenic protein was associated with a measurable rate of retrograde ejaculation, a condition that causes sterility. The researchers also looked at 243 of their own patients who underwent spinal fusion surgery post approval of Infuse and found retrograde ejaculation occurred in >7% of those treated with Infuse vs. <1% of those getting a standard graft.

The question being raised is whether Medtronic – along with doctors receiving money from the company – has downplayed this risk. In response, Medtronic said a higher rate of retrograde ejaculation with Infuse vs. control is listed in the product label.

This could complicate or delay a settlement between Medtronic and the Department of Justice over off-label promotion of Infuse.

NOVARTIS's Metopirone (metyrapone) – may help in PTSD

A 33-patient study published in the ***Journal of Clinical Endocrinology & Metabolism*** reported this drug – which is approved for use in the diagnosis of adrenal insufficiency – blocks cortisol, a stress hormone, and may be useful in treating post-traumatic stress disorder (PTSD). Subjects given a single dose of Metopirone three days after seeing a traumatic video had trouble recalling the story for at least several more days. When given a double dose, the subjects remembered even less of the negative parts of the story.

Paroxetine + pravachol – together they raise glucose

The combination of these two drugs, the first an antidepressant and the other a statin, appears to raise glucose levels significantly in a study reported in ***Clinical Pharmacology and Therapeutics***, though neither has this effect by itself.

The suggestion of this problem came from an analysis of the FDA's Adverse Event Reporting System (AERS) as well as data from Stanford, Harvard, and Vanderbilt universities. The researchers then tested the combination in mice and found the combination increased glucose from ~128 mg/dL to 193 mg/dL.

PFIZER

- **Aldactone (spironolactone)** – More than 2,000 bottles were recalled because the tablets were above specification at the 18-month stability time point.
- **Parexel International** and **Icon** were named as preferred providers of clinical trial implementation services. The partnership, which will be implemented over the next 18-24 months, is designed to help speed up drug research and make it more cost-effective.

Puerto Rican pharma manufacturing – under investigation

Politico reported that Rep. Darrell Issa (R-CA), chairman of the House Oversight and Government Reform Committee, traveled to Puerto Rico in an expansion of his committee's probe of **Johnson & Johnson**'s recall of Motrin, which is manufactured there. According to ***Politico***, four FDA officials flew to Puerto Rico to meet with Rep. Issa, who also wanted to talk with the San Juan district director of the FDA's Office of Regulatory Affairs.

After the trip, Rep. Issa sent a letter to FDA Commissioner Margaret Hamburg, MD, criticizing the FDA's supervision of the J&J plant and complaining that the FDA district director did not answer his questions adequately about steps to fix the issues at the plant. Rep. Issa also called it "unacceptable" that neither Dr. Hamburg nor her staff had been to the plant since September 2010.

Manufacturing problems keep popping up in Puerto Rico, and it is surprising Congress hasn't investigated sooner. This congressional investigation could have implications for other pharmas.

Sanofi – paid societies to lobby against generic Lovenox

The Senate Finance Committee found Sanofi paid two medical societies – the Society of Hospital Medicine and the North American Thrombosis Forum – and a researcher more than $5 million to lobby against approval of a generic version of Sanofi's Lovenox (enoxaparin), including filing a Citizen Petition with the FDA. The medical societies never disclosed the payments in their letters to the FDA.

Committee Chairman Max Baucus (D-MT) and Sen. Charles Grassley (R-IA) called on the FDA to require financial disclosure in such petitions and asked FDA Commissioner Dr. Hamburg what steps the FDA has taken "to ensure the integrity and transparency" of the lobbying process.

VARIAN MEDICAL SYSTEMS

- **Clinac and TrueBeam High Energy Linear Accelerator Models H14, H19, and H29**, which are used for stereotactic radiosurgery and precision cancer radiotherapy, were recalled because the coolant may leak, presenting a potential risk of electrical shock to someone working within the protective housing.
- **CENTELLA THERAPEUTICS' CEN-209 (formerly SN-30000)** – Varian got an exclusive license to this drug, which is designed to enhance the effectiveness of radiotherapy and chemotherapy when treating solid tumors that are hypoxic and, therefore, resistant to standard forms of radiotherapy and chemotherapy, from **Auckland UniServices** of New Zealand. In addition, Cancer Research UK (a U.K. charity) and Cancer Research Technology (the charity's development and commercialization arm) agreed to partner with Centella on the development, manufacturing, and testing of this cancer therapy for solid tumors.

VERTEX PHARMACEUTICALS' Incivek (telaprevir) – got FDA approval

Incivek was approved by the FDA to treat chronic hepatitis C virus (HCV) in combination with ribavirin and pegylated interferon. Incivek costs $49,200 for 12 weeks of treatment, but Vertex said it will provide the drug free to people with no insurance and a household income <$100,000/year and will have a copay assistance program for patients with commercial insurance.

Last week, the FDA approved Merck's Victrelis (boceprevir), the first direct-acting antiviral to treat people infected with HCV, so there are now two new direct-acting antivirals available to treat HCV. In a teleconference with various stakeholders, FDA officials discussed the efficacy and the safety of both of these drugs. There wasn't anything really new in the information, but some of the questions and answers are interesting.

FDA Commissioner Dr. Hamburg said that the two newly approved drugs "will make a difference, literally saving lives." Debra Birnkrant, MD, director of the FDA's Division of Antiviral Products, added, "This time reminds me of the mid-1990s when we approved various antivirals for the HIV-infected population and the impact those drugs had on patients' lives. We expect a similar result [with these drugs]. It is truly an exciting time."

Asked if it matters what type of food is eaten when these drugs are taken, Dr. Birnkrant said, "Food has an effect on absorption and plasma concentration, so it is recommended that patients take telaprevir three times a day with food that is not low fat. It could be a meal or snack but should not be low fat. Examples include bagels with cream cheese, nuts, granola, avocados… What's recommended for boceprevir could be a snack, but the high fat requirement is not needed for boceprevir."

Asked about the different futility rules for the two drugs – stopping Victrelis triple therapy at Week 12 if the viral load is ≥100, but not stopping Incivek unless it is >1,000 at Week 12 – Jeffrey Murray, MD, deputy director of the FDA's Division of Antiviral Products, explained, "The futility rules were based on looking at the data from the clinical trials…In [the Victrelis] database, we don't think that you're giving up any SVR – by giving up at Week 12." Dr. Birnkrant added, "Patients with inadequate viral response may develop treatment resistance…With telaprevir there are still some patients between 100 and 1,000 who still had an SVR."

What are the instructions for when a patient misses a dose? An FDA official said, "Talk to a physician about how to resume therapy. It is clearly stated in the label what to do."

Asked when the summary basis of approval will go up on the web, Dr. Birnkrant said, "I don't have an exact time frame, but, given the high visibility of these drugs, it should be expedited. Both labels are up, and both approval letters are online."

Asked if there are any follow-on data that will give patients and providers more guidance on how to incorporate these drugs into their clinical decision making, Dr. Murray said, "One of the post-marketing agreements is to look at IL28B and potential shorter durations of therapy, so we'll hopefully be getting a protocol for that relatively soon."

Asked about the effect of vitamin D and vitamin D products on SVR, Dr. Murray said, "We don't have any further information on that. You won't see it in the summary reviews. I don't think vitamin D levels were specifically measured."

Asked how clinicians should choose between the two drugs, Dr. Birnkrant said, "The only way we would be able to answer that is if they were compared in a head-to-head trial, which they were not. You have to consult future treatment guidelines… [Clinicians and patients] should read the prescribing information quite thoroughly. When the…other memos are up online, read those as well, and perhaps await recommendations from the professional organizations."

Is triple therapy the new standard of care? Dr. Birnkrant said, "The advisory committee clearly stated there was a new standard of care now, with these two direct-acting antivirals. So, it appears as though there is a new standard of care. Again, we have to await professional organization treatment guideline recommendations to see what these professional societies are recommending."

Asked about the timeline for data on HIV/HCV co-infected patients, Dr. Birnkrant said, "For telaprevir, as part of the post-marketing commitments, we asked the company to conduct a trial to look at [this]. The final protocol must be submitted by January 2012, and the trial is estimated to be completed by June 2014, with a final report by December 2014. There is a pilot study [in co-infected patients] in progress as well."

Asked about genotype-2 patients who relapse after treatment, Dr. Birnkrant said, "For telaprevir, pilot studies were conducted in other genotypes, and it didn't appear that it had adequate activity in any other genotype but 1a and 1b."

REGULATORY NEWS

FDA faces 11.5% budget cut

The House Appropriations Committee's 2012 spending bill includes a ~$285 million cut in FDA funding. With the fees it collects from industry, the Agency budget for next year would be ~$3.7 billion.

FDA oversight of annuloplasty rings criticized

In 2001, the FDA reclassified annuloplasty rings, which are used in heart valve repairs, from Class III devices to Class II, allowing them to be approved through the 510(k) process without clinical trials. Some experts are now raising concerns about the safety of these devices and the FDA's decision to down-classify them.

The ***Chicago Tribune*** reported annuloplasty rings have been linked to more deaths during the past five years than other Class II devices, though it is unclear whether that is due to the performance of the rings, the morbidity of the patients, or other factors.

Who petitioned the change? According to the ***Tribune***, it was the Advanced Medical Technology Association (AdvaMed).

The newspaper article said more than 700 patients got one of two rings made by Edward Lifesciences – IMR ETlogix and Myxo ETlogix (later renamed dETlogix) – that never even got 510(k) approval, ostensibly because they were "substantially equivalent" and did not require approval. However, the paper said Edwards filed patents for Myxo, claiming "dozens of ways in which it was different" from existing devices. Eventually, the FDA said the rings should have been cleared by the Agency first, but the paper said there was no penalty for Edwards.

FDA sets new financial disclosure rules

The FDA issued new draft guidelines for what pharmas and device companies will have to disclose about their financial relationships with investigators who work on drug and device studies, whether in the U.S. or abroad, including:

- Compensation the investigators get from any sponsor.
- The investigators' interest in patents, trademarks, and/or licenses.
- The sponsors' equity interests.

Companies also would have to disclose any research conducted domestically and abroad.

FDA to publish inspection records and letters

The FDA launched an online database that summarizes observations made during its inspections of manufacturing sites for drugs, food, and medical devices. In addition, within a few months, the FDA plans to start disclosing more warning letters regarding illegal product marketing.

European regulatory approvals

- **APTUS ENDOSYSTEMS' Aptus EndoStapling System** for endovascular aneurysm repairs received a CE Mark.
- **ELIXIR MEDICAL's DESyne**, a novolimus drug-eluting stent, received a CE Mark.
- **MEDTRONIC** received CE Mark approval to use its 16-electrode, fully implantable system for the percutaneous delivery of peripheral nerve stimulation (PNS) for the management of chronic back pain. The system will be incorporated into Medtronic's neurostimulation business. PNS is not approved in the U.S.

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

- **Cryoablation** – NICE plans to evaluate the use of percutaneous balloon cryoablation to treat atrial fibrillation.
- **DYSISMEDICAL's DySIS** – NICE will review this and other alternative colposcopy systems.
- **MEDTRONIC's deep brain stimulation (DBS)** – NICE plans to evaluate this epilepsy treatment.
- **ROCHE's MabThera/Rituxan (rituximab)** – NICE decided the evidence supports coverage of this monoclonal antibody to treat follicular non-Hodgkin's lymphoma.

Other recent FDA approvals and clearances

- **BIOMERIEUX's NucliSENS EasyQ MRSA,** a molecular test that can spot seven types of methicillin-resistant *Staphylococcus aureus* (MRSA), received 510(k) clearance.
- **OCEANA THERAPEUTICS' Solesta** – a sterile, injectable gel to treat fecal incontinence in patients for whom other therapies (e.g., diet, fiber, or anti-motility medications) have failed.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	May 2011	
May 30	**Optimer Pharmaceuticals' fidaxomicin** for the treatment of *C. diff*	PDUFA date
	June 2011	
June 2-3	Approaches and endpoints for devices for **seizure detection, cognitive evaluation, and traumatic brain injury/concussion assessment**	Joint workshop of the FDA, the American Academy of Neurology, the American Epilepsy Society, and the National Academy of Neuropsychology
June 8-9	**Reprocessing medical devices**	FDA public workshop
June 17	**Regeneron Pharmaceuticals aflibercept** (VEGF Trap-Eye) for wet AMD	FDA's Dermatologic and Ophthalmic Drugs Advisory Committee
June 17	**Celgene's Istodax** (romidepsin) – sDNA for peripheral T-cell lymphoma	PDUFA date
June 17	**Pfizer/King Pharmaceuticals' Acurox** (immediate-release oxycodone), a painkiller	PDUFA date
June 20	**Salix Pharmaceuticals' Xifaxan** (rifaximin) for non-constipation IBS	Company to meet with FDA on complete response letter
June 21	**Novartis's 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
	Other 2011 meetings/events	
July 11	**Novartis's Arcapta Neohaler** (indacaterol) long-acting beta agonist (LABA) for COPD	PDUFA date
July 20	**AstraZeneca's Brilinta** (ticagrelor), an anticoagulant	PDUFA date
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
2H11	**Abbott's RX Acculink** carotid stent	FDA final decision expected
Summer	Report on **FDA 510(k) reform**	Institute of Medicine
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
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