TRENDS-in-MEDICINE

November 4, 2012

by Lynne Peterson

Quick Takes

…Highlights from this week's news relating to drugs and devices in development that are not covered in other *Trends-in-Medicine* reports…

Trends-in-Medicine
Stephen Snyder, *Publisher*
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409
Fax 772-334-0856
www.trends-in-medicine.com
TrendsInMedicine@aol.com

NOTE: Subscribe to ***Trends-in-Medicine*** for coverage of the **American Heart Association** meeting in Los Angeles.

SHORT TAKES

- **AERIE PHARMACEUTICALS' AR-13324 –** The company announced positive top-line results from a Phase IIa trial of this investigational once-daily glaucoma treatment, with no serious adverse events. The company now plans a Phase IIb study.
- **ALLERGAN's Lap-Band –** The company said it is looking to sell this weight-loss product as sales continue to fall and controversies about efficacy and safety swirl.
- **AMERIDOSE**, a sister firm to the **New England Compounding Center** (which is at the center of the meningitis outbreak), recalled all of its unexpired products and will remain closed until at least November 19, 2012. Janet Woodcock, MD, director of the FDA's Center for Drug Evaluation and Research (CDER), said a preliminary FDA inspection raised concerns about the "sterility assurance" of the company's products and advised healthcare professionals to stop using all Ameridose products. The recall includes two critical care drugs that were already in short supply, and Dr. Woodcock said the FDA is "working with alternative manufacturers to maintain supplies."
- **BAYER** is buying **Schiff Nutrition International**, a nutritional supplement company, as part of its effort to diversify away from its core prescription drug operations and to expand its consumer-health footprint in North America.
- **BAYER and ONYX's Stivarga (regorafenib, BAY-73-4506)** received priority review status from the FDA to treat gastrointestinal stromal tumors (GIST).
- **BIOCRYST PHARMACEUTICALS' BCX-5191 –** The company withdrew its application to test this investigational NS5B nucleoside analog for treating hepatitis C after the FDA said it was concerned about toxicity.
- **BOEHRINGER INGELHEIM's Pradaxa (dabigatran) –** The FDA said its safety review of insurance claims and administrative data from its Mini-Sentinel pilot project indicates that the risk of serious bleeding with Pradaxa is no higher than with new use of warfarin. The FDA is continuing to review the safety of this drug but is not changing its recommendations about its use.
- ***British Medical Journal* (BMJ)** said that starting in January 2013, it will not publish the results of clinical trials unless the pharmaceutical companies and researchers agree to provide detailed study data on request.

- **CELLDEX THERAPEUTICS' CDX-1401** – The company reported positive results from a 45-patient Phase I study of this cancer vaccine targeting dendritic cells in patients with melanoma and other solid tumors.

- **COAXIA's NeuroFlo catheter** – The FDA's Neurological Devices Advisory Committee was due to review this device for treating patients with an ischemic stroke on November 1, 2012, but the meeting was postponed due to Hurricane Sandy. The FDA has not set a new date for the panel, and the company ran out of money waiting for FDA approval.

- **Colorectal cancer (CRC)** – A study published in the ***New England Journal of Medicine*** found that aspirin significantly improved survival in CRC patients with the PIK3CA mutation, so the mutation can serve as a biomarker to predict response in patients with newly diagnosed CRC. In the study, patients with the PIK3CA mutation had significantly longer cancer-specific survival with regular aspirin intake (hazard ratio 0.18 vs. non-aspirin users).

- **CORNERSTONE THERAPEUTICS' lixivaptan** – The FDA rejected this investigational drug to treat hyponatremia, saying more clinical and non-clinical information is needed. The company plans to meet with the FDA to clarify better what data will be needed.

- **DAINIPPON SUMITOMO PHARMA/SUNOVION PHARMACEUTICALS' Latuda (lurasidone)** – The company said the FDA accepted its application to expand the indication for this schizophrenia drug for use in treating bipolar disorder. The PDUFA date is June 20, 2013.

- **EXAGEN DIAGNOSTICS' Avise SLE diagnostic test** – New York state gave the company permission to distribute this lupus test across the state.

- **GI DYNAMICS' EndoBarrier** – The company received FDA permission to conduct a pivotal ~500-patient trial (ENDO) of this gastrointestinal liner in obese Type 2 diabetics. The trial could be the basis for a premarket approval application.

- **Henry Ford Health System** and **Beaumont Health System**, two Michigan hospital systems, are merging.

- **NAVIDEA BIOPHARMACEUTICALS' Lymphoseek (technetium-99m, tilmanocept)** – The FDA rejected this radioactive agent used to trace lymph nodes in cancer patients in September 2012, citing current good manufacturing practice (cGMP) issues related to the third-party contract manufacturer. The company resubmitted Lymphoseek, saying it has addressed the FDA's concerns.

- **SANOFI/GENZYME's Lemtrada (alemtuzumab)** – ***The Lancet*** published the results of two successful Phase III trials in multiple sclerosis (MS). However, an accompanying editorial was critical of the company's decision to take **Campath** (a different dose of alemtuzumab), which was used to treat chronic lymphocytic leukemia (CLL), off the market earlier this year, with plans to rebrand it as Lemtrada and reintroduce it for MS at a higher price.

- **Stem cells** – A study by Duke University researchers, published in the ***Proceedings of the National Academy of Sciences***, found that, at least in mice, an unlimited supply of stem cells can be created and turned into any type of tissue. In this case, the stem cells were turned into cartilage. The researchers hope their findings can be turned into new treatments for cartilage injury and osteoarthritis.

- **TRANSTECH PHARMA's TTP-488** – The company said this investigational Alzheimer's drug showed "promise" in a Phase IIb trial, with a 5 mg daily dose leading to a 26% improvement in the level of cognitive decline over 18 months vs. placebo. The effect was greatest (a 46% benefit) in patients with mild Alzheimer's.

- **VIIV HEALTHCARE's dolutegravir** – ViiV is buying the rights from **Shionogi** to this and other HIV treatments it has developed with Shionogi, and Shionogi will get a 10% stake in ViiV.

NEWS IN BRIEF

American Society for Radiation Oncology (ASTRO) – 54th annual meeting

- **Roche/Genentech's Avastin (bevacizumab)**. The S5033 trial of Avastin plus chemoradiation for inoperable non-small cell lung cancer (NSCLC) has been stopped, at least temporarily, with just 29 patients enrolled after two of the first 7 patients developed fatal hemoptysis. In addition, there were other toxicities, including anemia, pneumonitis, and electrolyte abnormalities. Yet, the combination did show some preliminary evidence of activity.

- **SalutarisMD**. A six-patient study found that a single dose of the company's investigational retrobulbar episcleral brachytherapy, added to intraocular VEGF inhibitor injections, in patients with wet age-related macular degeneration (AMD) is feasible and tolerable, with "measureable and clinically meaningful improvement in visual acuity." No patients required additional anti-VEGF injections during the 90-day trial period.

- **Stereotactic radiation.** Japanese researchers reported that their 104-patient study found the use of stereotactic body radiation therapy (total 48 Gy) in inoperable early non-small cell lung cancer (NSCLC) led to longer 3-year and 5-year survival vs. historical controls. About 60% of the patients achieved 3-year overall survival, with 40.8% alive at 5 years.
- **Xoft's Axxent Electronic Brachytherapy.** Data from a 122-patient study suggested that non-melanoma skin cancer (even in hard-to-treat areas) can be safely removed with this external radiation therapy, given as outpatient therapy. Cosmesis was rated as good, and the most common adverse event, occurring in 13% of patients at 2 years, was hypopigmentation. At a mean follow-up of 11 months, no patients had a recurrence.

AMGEN's Prolia (denosumab) – favorable study results

- Researchers reported in the ***New England Journal of Medicine*** on two case studies that suggest this osteoporosis drug may help control calcium levels after a stem cell transplant for osteopetrosis.
- Three-year results from the 667-patient FREEDOM trial, published in the ***Journal of Bone and Joint Surgery***, indicated that Prolia does not impair fracture healing in women with osteoporosis who suffer a fracture. There was no increased risk of incomplete fracture healing in Prolia patients vs. placebo.

Antiplatelet drugs – new STS guidelines

The Society of Thoracic Surgeons (STS) updated its clinical practice guidelines for antiplatelet drugs in surgical patients (cardiac and non-cardiac). Among the key recommendations:

- Discontinuation of P2Y12 inhibitors – clopidogrel and **Lilly's Effient** (prasugrel) – a few days before cardiovascular operations (Class I, level of evidence B).
- Aspirin discontinuation before purely elective operations in patients without acute coronary syndromes (ACS) is reasonable to decrease the risk of bleeding.
- Use of point-of-care platelet function testing:
  - Is recommended prior to cardiac surgery (Class IIb, level B), but these tests have a limited positive predictive value, so they are best used for their negative predictive value in identifying patients with high residual platelet reactivity who will not be at elevated risk of bleeding during surgery.
  - Can help guide perioperative blood transfusions (Class IIb, level B). However, the reproducibility, accuracy, and correlation among various tests are variable and suboptimal.
- Ticagrelor (**AstraZeneca's Brilinta**) should not be started in non-STEMI patients who might have CABG.
- Antiplatelet drugs should not be given before cardiac surgery to patients (usually children) with hereditary platelet defects or to patients with acquired platelet defects (Class III, level C).
- It is reasonable to continue dual antiplatelet therapy (e.g., aspirin + clopidogrel) in stented patients undergoing noncardiac surgery (Class IIb, level C).
- A multidisciplinary approach to the use of antiplatelet drugs is strongly recommended for patients who require cardiac surgery (Class IIa, level B).
- For patients needing urgent surgery:
  - Delaying the operation for a day or two is reasonable in patients with ACS (Class IIa, level B).
  - It is reasonable to make decisions based on platelet inhibition tests (Class IIa, level B).
  - Bridging urgent patients with short-acting antiplatelet agents received a Class IIb recommendation (level B).
  - For ACS patients on dual antiplatelet therapy or with a drug-eluting stent for <1 year, the operation should proceed at intervals <5 days (Class IIb, level C).

BIOGEN IDEC and ORPHAN BIOVITRUM's recombinant Factor VIII Fc fusion protein (rFVIIIFc) – positive Phase III results

The companies reported that a 165-patient Phase III trial showed this investigational treatment for hemophilia A effec-tively prevented bleeding with fewer injections (1.6 bleeds with injections about once every 3.5 days vs. 3.6 bleeds with weekly injections and 33.6 bleeds when given as needed). Patients being treated with rFVIIIFc needed 1-2 injections per week vs. 3-4 injections a week with existing medications. The companies plan to submit rFVIIIFc to the FDA in early 2013. None of the patients developed inhibitory antibodies.

ENDO PHARMACEUTICALS' Opana ER – FDA investigating deaths

At the end of August 2012, the FDA received reports of at least 12 patients in Tennessee who developed thrombotic thrombocytopenic purpura (TTP), a rare and potentially fatal

blood disease, after injecting this painkiller for non-medical reasons. The FDA and the Centers for Disease Control and Prevention (CDC) are working with the Tennessee Department of Health to investigate. The FDA does not know whether the patients injected the previous formulation or the newer tamper-resistant formulation that replaced the older ER formulation since both are called Opana ER, but by the end of August, most of the older formulation likely would have been replaced by the newer formulation (sometimes referred to as Opana CR), at least in retail settings.

Flu tests – rapid tests very variable

A recent *Morbidity and Mortality Weekly Report* reviewed 11 FDA-approved rapid flu tests and found most tests detected viral antigens in samples with the highest viral concentrations, but:

- One test didn't uniformly detect high concentrations of influenza A viruses.
- Four tests detected at least 70% of B viruses in the third-highest concentration samples.
- One test detected at least 50% of influenza A viruses in the third-highest concentration samples.

The researchers said clinicians should collect respiratory specimens from patients within 24 to 72 hours of symptom onset, when the level of flu virus in the body is highest, and should not exclude a flu diagnosis in patients with symptoms of infection.

GLAXOSMITHKLINE

- **Tykerb (lapatinib) – shrinks breast cancer brain mets.** The Phase II LANDSCAPE trial found that combining Tykerb and **Roche's Xeloda** (capecitabine) shrank brain metastases in women with HER2+ breast cancer without using radiation. In the study, two-thirds of patients had shrinkage of ≥50% of their brain mets, delaying the need for whole-brain radio-therapy, which can impair cognitive function. However, Grade 3/4 adverse events (mostly diarrhea and hand-foot syndrome) were common with the therapy, occurring in 49% of women.
- **GSK/HUMAN GENOME SCIENCES' raxibacumab** – The FDA's Anti-Infective Drugs Advisory Committee voted unanimously to recommend approval of this investigational monoclonal antibody to treat inhalational anthrax. This was the company's second submission for this infused drug; the FDA turned it down three years ago. The panel also voted 18-0 that raxibacumab is effective in treating humans who inhale anthrax, and they voted 16-1 (with one abstention) that raxibacumab is effective. December 15, 2012, is the PDUFA date.

MYRIAD GENETICS – criticized for withholding data

An article in the ***European Journal of Human Genetics*** claimed that Myriad, which provides the BRCA1/2 genetic test, has amassed vast quantities of clinical data and hasn't shared that data. In response, Martina Cornel, MD, PhD, a Dutch geneticist and chair of the European Society of Human Genetics' Professional and Public Policy Committee, said: "We are very concerned that such important data are being withheld from those who most need it…By not sharing their data on the VUS (variants of unknown significance)…where Myriad is the sole commercial provider of a test in the U.S., geneticists have been unable to develop the up-to-date algorithms that are necessary to best interpret the effects of genetic variants. While Myriad has access to public databases in order to help interpret their VUS results, this is currently not reciprocal…What is particularly worrying about this situation is that it is the first time that such inequities have been based on a lack of access to clinical information, rather than lack of a product. Myriad's stated aim to enter the European market more vigorously may lead to unfair competition with academic institutions for predictive precision. It is vital that progress towards personalized medicine, which holds out so much promise, is not hindered by companies maintaining private genomic databases. Policymakers should take an urgent look at the regulatory and reimbursement issues involved in genomic testing."

NOVARTIS

- **Flu vaccines.** Canada and Switzerland lifted their bans on these vaccines, but other European countries are continuing to ban the vaccines because of white particles found in some vials.
- The company plans to build a new biotech production facility in Singapore, with construction to begin in early 2013.

QUESTCOR's Acthar (adrenocorticotropic hormone, ACTH) – potential U.S. competitor on the horizon

The FDA granted **Cerium Pharmaceuticals** orphan drug status for a generic version of **Synacthen Depot** [tetracosactide hexaacetate (beta 1-24-corticotropin)] – which is a synthetic version of Acthar – for infantile spasms. Cerium, which was chartered in March 2012 and does not even have a website, appears to be no more than a storefront. The office is a duplex converted to commercial space in Gaithersburg MD, and the founder is a former Questcor board member who has

also headed other small pharmaceutical companies (sometimes more than one at the same time), including Sigma-Tau and Klee Pharmaceuticals.

However, Cerium founder Gregg Lapointe has some very real credentials. He is a certified public accountant and has been a member of the Corporate Council of the National Organization for Rare Diseases (NORD), Child Neurology Foundation, Kidney Care Partners, and a board member for PhRMA (Pharmaceuticals Research and Manufacturers of America), SciClone Pharmaceuticals, and Soligenix.

Maybe the goal is to create a company to sell to Sigma-Tau.

SANOFI and REGENERON's SAR-236553 – boosts efficacy of Lipitor

A 92-patient, multicenter, double-blind Phase II study published in the ***New England Journal of Medicine***, found that at Week 8 this subcutaneous monoclonal antibody boosted the efficacy of **Pfizer's** Lipitor (atorvastatin) in lowering cholesterol:

- There was a 73% LDL reduction when combined with 80 mg atorvastatin and a 66% reduction when combined with 10 mg of atorvastatin vs. 17% on atorvastatin alone.
- Twice as many patients on SAR-236553 + 80 mg atorvastatin achieved LDL <100 mg/dL, and the number of patients reaching a target of <70 mgdL was five-fold greater with that combination.
- SAR-236553 + 80 mg atorvastatin significantly increased HDL by 5.8 mg/dL.
- Adverse events were not worse than atorvastatin alone.

TAURX THERAPEUTICS' LMTX (leuco-methylthioninium) – is now the time for a tau approach in AD?

The company recently announced the start of two Phase III trials of this second-generation tau aggregation inhibitor, given BID:

1. Mild-to-moderate Alzheimer's disease (AD) – a 12-month, 833-patient study in the U.S., eastern Europe, and Asia, with top-line results expected in April 2015.
2. Mild AD – an 18 month, 500-patient study mostly in the U.S. and Europe, with top-line results expected in October 2015.

The primary endpoint in both studies is ADAS-Cog_{11}. FDG PET imaging will be done in the trial, with volumetric MRI a secondary endpoint in the mild AD trial. Cerebral spinal fluid (CSF) testing for tau is optional for investigators, "If people [patients] are willing to agree to a lumbar puncture, we will analyze it, but we see it as purely exploratory science…I haven't a clue where tau in the CSF comes from…We did a lot of research on how tau is processed in the course of neurodegeneration, and it loses all its p-tau markers…So, whatever is being picked up in the CSF is not coming from advanced stages of neurodegeneration…and amyloid treatment seems to change the levels of tau…So, it is complicated."

The results from the ongoing frontotemporal dementia (FTD) trial are expected in February 2015.

In a webinar, Claude Wischik, MD, a psychiatrist and founder/CEO of TauRx, said it is now time to explore further the tau hypothesis in AD, "A great deal of money has been spent on the amyloid hypothesis, and to date there have been 17 failed Phase II and Phase III trials…The effect we have seen so far is fairly small [with anti-amyloid agents]…[Lilly's] solanezumab appears very similar to Aricept [Pfizer, donepezil, an acetylcholinesterase inhibitor]. The question is whether it is disease-modifying or simply delays cognitive decline – but there is a glimmer of hope there…We focus on the tangle/tau approach …looking to see if we can 'strangle' the tau…The time for tau is now."

Dr. Wischik said it is commonly thought that the tau pathway comes late in the disease process, but tau accumulation and tangles actually begin even earlier than beta-amyloid accumulation in the brain, "It is true to say the disease appears late, but the tau pathway begins 20-30 years before the disease becomes apparent…So, this is not something in the brain that is late… Once the tau process has begun in the brain, it is spread throughout the brain in an orderly way…LMTX stops that by dissolving the aggregates and stopping their ability to propagate themselves. LMTX stops the exponential progression of the disease."

In Phase II, rember (the first-generation tau inhibitor) reduced progression 85% overall, and 93% in mild AD patients. Dr. Wischik said regulators allowed the company to take LMTX into Phase II based on the rember data in Phase II. Compared to rember, LMTX is directly absorbed into the bloodstream with or without food, and it is better tolerated, so dosing was reduced.

Why hasn't the Phase II data been published yet? Dr. Wischik said, "This is often asked. The company took the strategic position not to publish until after we got regulatory approval for Phase III. We now have that in Europe and the U.S…We expect to publish in 2013."

In the end, Dr. Wischik said that AD patients may need both a tau aggregation inhibitor and a beta-amyloid inhibitor.

How long would patients need to take LMTX? Dr. Wischik said, "My suspicion is people will have to take it over the longer term…It is not a one-shot cure."

REGULATORY NEWS

Extended-release generics under FDA microscope

The FDA is taking a closer look at the way generic drug companies make extended-release drugs in the wake of the discovery that **Teva/Impax Laboratories**' 300 mg generic bupropion did not have the same efficacy as the same dose of the brand (**GlaxoSmithKline's Wellbutrin**). So far, the FDA has said the bupropion incident is unique and generic drugs are equivalent to brands, but Gregory Geba, MD, MPH, director of the FDA's Office of Generic Drugs, said, "This has actually prompted us to change our policy."

FDA's 510(k) device approval process beefed up

The FDA set new review timeframes and performance goals for 510(k) medical devices. By 2017, the FDA expects to gradually reduce the average time for 510(k) decisions to 124 days in 2017, down from 150 days in 2012.

Key performance goals include:

- For 2012 – clearance decisions within 90 days for 90% of submissions received and 150 days for 98% of submissions.
- Starting in 2013, even shorter review times – depending on new obligations on the FDA and on 510(k) applicants under MDUFA III.
- All submissions will have to include electronic copies of pertinent documents.
- The FDA will conduct a preliminary **Acceptance Review** within 15 calendar days of receiving a 510(k) application and will notify applicants of any Refuse to Accept (RTA) decisions if submissions are incomplete. Submissions subject to RTA decisions will be put on hold until applicants provide missing information.
- The FDA will conduct **Substantive Reviews** of 510(k) applications once those applications have passed the Acceptance Review phase.
- Only two rounds of review are planned for 510(k) submissions starting in fiscal year 2013, and the FDA will grant only one 180-day extension in the event of an additional information request.
- The FDA hopes to reduce decision timeframes steadily between 2013 and 2017, aiming for 135 days in 2013 and 2014, 130 days in 2015 and 2016, and 124 days in 2017.

FDA approvals/clearances

- **CARESTREAM HEALTH's lesion management module** for its Vue PACS workstation software was cleared for use.
- **JOHNSON & JOHNSON's Xarelto (rivaroxaban)** received expanded approval to include treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and to reduce the risk of recurrent DVT and PE after initial treatment.
- **LEO PHARMA's Taclonex (calcipotriene + betamethasone dipropionate)**, a once-daily topical suspension for treating patients with scalp plaque psoriasis, was approved to treat body plaque psoriasis as well.
- **MAQUET CARDIOVASCULAR's Sensation Plus 7.5Fr 40cc intra-aortic balloon catheter** received 510(k) clearance.
- **MEDTRONIC's Affinity Pixie Oxygenation System**, which provides lung support in pediatric, infant, and neonatal patients receiving open-heart procedures, received 510(k) clearance.
- **NUVASIVE's PCM cervical disc system** received FDA premarket approval.
- **PROVIDENCE MEDICAL TECHNOLOGY's PMT bone screws** received 510(k) clearance, and the company plans to launch the product in 1H13 for use in joint repair, bone reconstruction, etc.
- **THERMEDICAL's Thermedical Ablation System**, which was developed in part with grants from the National Institutes of Health (NIH), was cleared for ablation and coagulation of soft tissue during specific surgical procedures.
- **X-SPINE SYSTEMS' Fortex CoCr Rod System and Certex Cervico-thoracic Fixation System** – Both spinal implants were approved.

FDA recalls/warnings

- **ATRIUM MEDICAL** received an FDA warning letter that the plant where its stents, chest drains, and other medical devices are made is not in compliance with cGMP requirements.

- **HOSPIRA's Symbiq infusion system** – A Class I recall was initiated for these drug-delivery pumps because of inaccurate response of the touchscreen to user input.

European regulatory news

- **BLUE MEDICAL DEVICES' Protégé NC system**, a next-generation version of the company's Protégé drug-eluting balloon, was granted a CE Mark. The new device combines non-compliant balloon technology with a drug-eluting balloon.
- **BOSTON SCIENTIFIC's Synergy everolimus-eluting stent** with a bioabsorbable coating received a CE Mark. The company plans a limited launch in early 2013.
- **CARDIOKINETIX's Parachute heart implant** – The company received a CE Mark for all eight sizes of this ventricular partitioning system designed to offer support to patients with weakened cardiac muscles.
- **C8 MEDISENSORS' Optical Glucose Monitor System**, which measures blood glucose non-invasively and wirelessly transmits glucose readings to smartphones, received a CE Mark.
- **MAQUET CARDIOVASCULAR's Sensation Plus 7.5Fr 40cc intra-aortic balloon catheter** received a CE Mark.
- **NOVARTIS' Seebri (glycopyrrolate bromide)** – The European Medicines Agency (EMA) said that clinical trial data suggest this chronic obstructive pulmonary disease (COPD) drug is more effective taken 25 mg BID than 50 mg QD. Therefore, the EMA asked Novartis to do an additional study in humans to find the optimal dosing schedule. The FDA also requested more data on Seebri.
- **ROCHE's Avastin (bevacizumab)** – The European Commission approved use in combination with standard chemotherapy (carboplatin and gemcitabine) to treat women with a first recurrence of platinum-sensitive ovarian cancer.
- **SEATTLE GENETICS and TAKEDA/MILLENNIUM's Adcetris (brentuximab vedotin)** received conditional marketing approval to treat Hodgkin's lymphoma and systemic anaplastic large cell lymphoma.

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

- **BRISTOL-MYERS SQUIBB's Yervoy (ipilimumab)** – NICE recommended use of this melanoma drug post-chemotherapy by the National Health Service (NHS) after the company dropped the price, which had been £75,000 ($120,000) for a four-dose course. The amount of the discount was not disclosed.
- **ROCHE's Zelboraf (vemurafenib)** – NICE recommended use of this melanoma drug in BRAF+ patients by the NHS after the company dropped the price, which had been £52,500 ($84,000) for the 7-month treatment course. The amount of the discount was not disclosed.

Regulatory news from other countries

Brazil: In an effort to boost manufacturing competitiveness, the government introduced legislation that would lower the social security contributions required by medtech companies for two years (January 1, 2013, through December 31, 2014).

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	2012	
TBA	**CoAxia's NeuroFlo** catheter for treating cerebral ischemia	FDA's Neurological Devices Advisory Committee ***Postponed from November 1 due to weather***
November 7	**Novartis' Signifor** (pasireotide) to treat Cushing's disease	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
November 8	**Novo Nordisk's Tresiba** (degludec) **and Ryzodeg** (degludecPlus)	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
November 9	**MSD Consumer Care's "Oxytrol for Women,"** an over-the-counter transdermal oxybutynin to treat overactive bladder in women	FDA's Non-prescription Drugs Advisory Committee
November 14	Optimization of outcomes with **ventricular assist devices** (VADs) for patients with heart failure	CMS' MEDCAC
November 21	**Pfizer's tofacitinib**, an oral JAK inhibitor for rheumatoid arthritis	PDUFA date (extended from August 21)
November 28	**Johnson & Johnson's bedaquiline** to treat patients with multi-drug resistant pulmonary tuberculosis	FDA's Anti-infective Drugs Advisory Committee
November 28	Discussion of the use of **absorbable material** in a variety of medical devices	FDA Workshop on Absorbable Medical Devices: Lessons Learned From Correlations of Bench Testing and Clinical Performance
November 29	**Exelixis' cabozantinib** to treat medullary thyroid cancer	PDUFA date
December 4	Discussion (no votes) of pediatric development plans for **GlaxoSmithKline's trametinib, Threshold Pharmaceuticals' TH-302, Boehringer Ingelheim's volasertib** (BI-6727)**,** and **Amgen's blinatumomab** (MT-103)	FDA's Pediatric Oncology subcommittee of the Oncologic Drugs Advisory Committee (ODAC)
December 15	**Human Genome Sciences' raxibacumab** to treat inhalation anthrax	PDUFA date
December 20 **confirmed**	**Hemispherx Biopharma's Ampligen** (rintatolimod injection, poly I: poly C12U) to treat chronic fatigue syndrome (CFS)	FDA's Arthritis Advisory Committee
December 21	**Alexza Pharmaceuticals' Adasuve** (loxapine) for agitation associated with schizophrenia or bipolar disorder	PDUFA date
December 29	**Aegerion Pharmaceuticals' lomitapide** to treat homozygous familial hypercholesterolemia	PDUFA date
December 29	**Johnson & Johnson's bedaquiline** to treat multi-drug resistant tuberculosis	PDUFA date
December 30	**NPS Pharmaceuticals' Gattex** (teduglutide) for short bowel syndrome	PDUFA date
	2013	
January 16	**Santarus' Uceris** (budesonide) for ulcerative colitis	PDUFA date (extended from October 16, 2012)
January 17	**NuPathe's Zelrix** (transdermal sumatriptan), a migraine patch	PDUFA date
January 21	**Impax Laboratories' Rytary** (IPX-066) for Parkinson's disease	PDUFA date (extended from October 21, 2012)
January 29	**Sanofi/Genzyme** and **Isis Pharmaceuticals' Kynamro** (mipomersen) for homozygous familial hypercholesterolemia	PDUFA date
January 30	**Raptor Pharmaceutical's cysteamine bitartrate** delayed-release (RP-103) to treat nephropathic cystinosis	PDUFA date
February 2	**Hemispherx Biopharma's Ampligen** (poly I: poly C12U) to treat chronic fatigue syndrome	PDUFA date
February 10	**Celgene's pomalidomide** for relapsed/refractory multiple myeloma	PDUFA date
February 24	**Dynavax's Heplisav** hepatitis B vaccine	PDUFA date
February 28	**Lundbeck** and **Otsuka's aripiprazole depot** to treat schizophrenia	PDUFA date
March tba	**Johnson & Johnson's canagliflozin**, a SGLT2 inhibitor to treat Type 2 diabetes	PDUFA date
March 1	**Zogenix's Zohydro** (extended-release hydrocodone) for chronic pain	PDUFA date
March 17	**Bristol-Myers Squibb** and **Pfizer's Eliquis** (apixaban,) an oral anticoagulant to prevent stroke in atrial fibrillation patients	PDUFA date
March 27	**Ariad Pharmaceuticals' ponatinib** for treatment-resistant leukemia	PDUFA date
March 28	**Biogen Idec's BG-12** (dimethyl fumarate) for multiple sclerosis	PDUFA date (extended from December 28, 2012)

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
	more 2013	
April 11	**Sanofi/Genzyme** and **Bayer's Lemtrada** (alemtuzumab) for multiple sclerosis	PDUFA date canceled because the FDA refused to accept the filing
April 29	**Shire's Vyvanse** (lisdexamfetamine dimesylate), sNDA for ADHD treatment in children	PDUFA date
May 12	**GlaxoSmithKline** and **Theravance's Breo/Relvar** (fluticasone furoate + vilanterol) to treat chronic obstructive pulmonary disease (COPD)	PDUFA date
May 31	**DepoMed's Serada** (gabapentin extended-release), a hot-flash treatment	PDUFA date
June 20	**Dainippon Sumitomo Pharma/Sunovion Pharmaceuticals' Latuda** (lurasidone), a schizophrenia drug for use in treating bipolar disorder	PDUFA date
July 28	**Aveo Oncology** and **Astellas Pharma's tivozanib** to treat advanced renal cell carcinoma	PDUFA date