Trends-in-Medicine

Quick Takes

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Trends-in-Medicine
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Check out the new *Trends-in-Medicine* blog on our website (www.trends-in-medicine.com). The latest entry is about traveling to medical conferences.

…Highlights from this week's news affecting drugs and devices in development…

SHORT TAKES

- **AVEO PHARMACEUTICALS' tivozanib** has been granted orphan drug status by European regulators.
- **CADENCE PHARMACEUTICALS** has signed an option to buy Incline Therapeutics at a cost of $135 million during the first option period or $228 million during the second option period, plus an additional payment of up to $57 million if the Ionsys postsurgical pain treatment system gains FDA approval. (*More information is available at:* **www.bizjournals.com/sanjose/stories/2010/06/21/daily12.html**.)
- **EXELIXIS** and **BRISTOL-MYERS SQUIBB** have ended their development partnership for XL-184, a potential thyroid cancer therapy, which now returns to Exelixis. Phase III data are expected to be released early in 2011.
- **GLAUKOS's iStent** for use in conjunction with cataract surgery in patients with open-angle glaucoma will be reviewed by the FDA's Ophthalmic Devices Advisory Committee on July 30, 2010.
- **GW PHARMACEUTICALS' Sativex (nabiximols, GW-1000)**, an oral (buccal) spray, was approved by the U.K. Medicines and Healthcare Products Regulatory Agency to treat spasticity associated with multiple sclerosis, making it the first prescription drug made from cannabis to be officially marketed anywhere in the world. It is also being developed for use in patients with pain due to cancer and in those with neuropathic pain.
- **JAZZ PHARMACEUTICALS' Xyrem (sodium oxybate, JZP-6)** is scheduled for review by a joint meeting of the FDA's Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee on August 20, 2010.
- **MELA SCIENCES' MelaFind**, a non-invasive computer vision system intended to help physicans evaluate whether skin lesions and moles are suspicious enough for melanoma to warrant a biopsy, will be reviewed by the FDA's General and Plastic Surgery Devices Advisory Committee on August 26, 2010.

- **SKYEPHARMA's Flutiform (fluticasone/formoterol) –** The FDA wants more clinical trial data before it will approve this asthma treatment, which Skye said may kill the drug.
- **VALEANT PHARMACEUTICALS** and **BIOVAIL** estimate that they will realize $175 million in savings within two years as a result of their $3.2 billion merger, in which the new company will retain the Valeant name and focus on dermatology and neurology products as well as branded generics.
- **ZIOPHARM's palifosfamide –** A clinical trial in patients with unresectable or metastatic soft tissue sarcoma is being delayed because of FDA concerns about the study design.

NEWS IN BRIEF

ABBOTT/BIOGEN IDEC's daclizumab – Phase III trial started

In May 2010, the first of the expected 1,500 patients was enrolled in a Phase III multiple sclerosis trial of daclizumab, an injected therapy. The primary investigator is Dr. Ludwig Kappos of Switzerland.

AFFYMAX's Hematide (peginesatide) – safety results mixed

Results of Phase III studies of this potential anemia treatment revealed higher rates of cardiac side effects, including unstable angina, rhythm abnormalities, and higher rates of death among a subgroup of patients with kidney disease not requiring dialysis. ***Bloomberg News*** reported that these results may delay the company in seeking approval for Hematide. Currently, Amgen's Aranesp (darbepoetin alfa injection) is a mainstay treatment for anemia in patients with kidney disease. The clinical trial results did show, however, that Hematide was as effective as Aranesp, which was associated with lower rates of cardiac side effects.

Autologous stem cells – restore sight after ocular burn

Italian researchers reported in the ***New England Journal of Medicine*** that a limbal stem cell transplant permanently restored normal vision in 21 of 46 patients and restored partial vision in the others. The results were long-lasting, but the transplant only worked for patients who had at least some viable limbal cells left in one of their eyes.

AVID RADIOPHARMACEUTICALS' florbetapir – new contrast agent

A clinical trial with 11 Alzheimer's disease patients and 15 controls showed that this contrast agent had strong and consistent binding to the beta-amyloid plaques in the brains of Alzheimer's patients and may be a practical agent for use with PET scans to help identify and monitor progression of the disease. Although there is no indication that florbetapir is superior to Pittsburgh Compound B (PiB), researchers predicted it may eventually replace PiB as a contrast agent. However, florbetapir has a longer half-life (2 hours) vs. a few minutes for PiB, which may make florbetapir a more practical choice.

BIOGEN IDEC/ELAN's Tysabri (natalizumab) – PML cases mount

As of June 7, 2010, ~68,000 multiple sclerosis patients were on Tysabri, 55 had developed PML (progressive multifocal leukoencephalopathy), and 11 PML patients had died. The incidence is still below the 1:1,000 that the FDA had set for a positive benefit:risk profile, but it is continuing to get closer to the point where it may no longer have acceptable safety.

BIOSANTE's LibiGel (transdermal testosterone gel) – development continues

A Phase II clinical trial showed that this topical treatment significantly increased the number of satisfying sexual events among menopausal women with sexual dysfunction compared to placebo. The company plans to pursue Phase III clinical trials with LibiGel following a review of the safety data.

Bisphosphonates – may lower risk of invasive breast cancer

In two studies published in the ***Journal of Clinical Oncology***, researchers reported that the risk of invasive breast cancer declined 30%-40% among postmenopausal women who were taking bisphosphonates. In the Women's Health Initiative (WHI) trial, women on bisphosphonates had a 32% reduction in breast cancer risk over the nearly 8 years of follow-up. An Israeli study found a 39% relative risk reduction among women who took a bisphosphonate for at least 1 year, and women who did get breast cancer tended to have more favorable prognostic characteristics. *This is not an entirely new idea or finding, but the evidence appears to be building.*

Blood clotting – genes found

Researchers from Harvard Medical School and Johns Hopkins University have identified 7 genes that are 500 million times more likely than other genes to regulate blood platelet clotting. They said the proteins produced by the 7 genes may be used to develop tests that will help identify which patients will respond to the anticoagulant medications that are used extensively in patients following cardiac procedures. In addition, the findings may lead to the development of new treatment targets for arterial disease and wound healing. (The study appears in the online edition of ***Nature Genetics***.)

BOEHRINGER INGELHEIM's Girosa (flibanserin) – FDA panel rejects it

The FDA's Reproductive Health Drugs Advisory Committee didn't like either the safety or the efficacy of Girosa, a once-a-day pill designed to be taken at bedtime by premenopausal women with persistent, bothersome, and unexplained lack of sex drive. The panel voted 11-0 that Girosa's risks (depression, fainting, fatigue, etc.) were unacceptable and 10-1 that efficacy data were lacking. The panel chair, Dr. Julia Johnson, an ob/gyn from the University of Massachusetts Medical School, said, "The efficacy was not sufficiently robust to justify the risks."

Originally developed as an antidepressant and believed to act on brain chemicals that play a role in sexual response, Girosa was the latest attempt to find a female counterpart to Pfizer's Viagra (sildenafil). Dr. Leonore Tiefer, a psychiatrist from New York University, read from a petition opposing approval of Girosa, saying, "Low sexual desire is not a disease."

While the panel decided the drug "isn't ready for prime time," it did agree that hypoactive sexual-desire disorder (HSDD) is a legitimate medical disorder that "deserves an FDA-approved treatment."

Cyclosporine – increased cancer risk in liver transplant patients

In a study published in ***Liver Transplantation***, Dutch researchers reported that transplant patients taking cyclosporine (CsA) have a significantly increased risk for development of *de novo* cancer. While the 1-year survival has dramatically increased and is now >80% in liver transplant patients, there has been little improvement in long-term outcomes, largely due to cancer deaths which appear to be directly related to the intensity and cumulative dose of cyclosporine.

The researchers did a retrospective analysis of 385 liver transplant patients, looking at *de novo* malignancy (defined as the development of cancer other than recurrent primary liver cancer), and they found 13.0% developed at least one *de novo* cancer. They also found that the key cancer risk factors were: age <50, use of cyclosporine instead of tacrolimus (Astellas's Prograf) for immunosuppression. Cyclosporine patients also had more aggressive types of cancer compared to tacrolimus patients, with a 1-year survival rate <30%.

They believe the reason for the increased cancer rates among cyclosporine recipients is the change in cyclosporine monitoring policy that occurred in 2005 – a shift from C_0 level monitoring to dosing based on C_2 level monitoring. Dr. Herold Metselaar, the team leader, said, "Strikingly, cyclosporine-treated patients transplanted from 2005 on showed a 9.9-fold higher *de novo* cancer risk in the early phase after liver transplant compared to patients treated with tacrolimus. These data indicate that only the specific CsA treatment used in recent years was associated with a higher risk for early development of *de novo* cancer...We also observed that, compared with tacrolimus-treated patients, cyclosporine-treated patients had a 2.5-times higher risk to develop more aggressive cancer types that do not belong to the non-melanoma skin cancer and post-transplant lymphoproliferative disorder (PTLD) categories, indicating that cyclosporine is not only associated with a higher early *de novo* cancer risk but also with cancer types having a worse prognosis."

In an accompanying editorial, Dr. Julie Thompson, a gastroenterologist from the University of Minnesota, called for further study, "These data serve as a call to reassess the aggressiveness of current immunosuppressive regimens as a means of reducing risk from *de novo* malignancy."

Deuterium depletion – a new approach to cancer therapy?

At the 1st International Symposium on Deuterium Depletion last month in Budapest, Hungary, the focus was on advances in the research and clinical application of deuterium depletion, its present and future role in anticancer research, oncotherapy, diabetes, and anti-aging. Researchers from the U.S., Hungary, Romania, Russia, and Iran discussed current advances in the research applications of deuterium depletion, which was invented by a Hungarian scientist, Gabor Somlyai, PhD. Among the research findings were reports that:

- Manganese caused a shortened lifespan in worms that was reversed by deuterium-depleted water.
- Decreased deuterium to hydrogen ratios regulate sterol and fatty acid precursor synthesis, which probably affects the rate of divisions and cellular proliferation via limited reductive synthesis and new membrane formation.
- Exposure to deuterium-depleted doxorubicin variants significantly increased apoptosis induction of HT-29 cells vs. normal doxorubicin.

The conference was organized by Hyd, a Hungarian pharmaceutical company, which plans to start a Phase II trial later this year of deuterium-depleted water in symptomatic, naïve chronic lymphocytic leukemia (CLL) patients. GlaxoSmith-Kline (GSK) is collaborating with Concert Pharmaceutical on deuterium-containing drugs, including: CTP-518, a protease inhibitor for the treatment of HIV; a preclinical compound for chronic renal disease; and an unspecified third product from Concert. Concert is also providing GSK with deuterium-modified versions of three unspecified GSK pipeline compounds for GSK to develop.

Digoxin – excess death in patients on dialysis

Results of a huge study showed that digoxin use was associated with an increased risk of premature death in kidney disease patients requiring dialysis. The results were reported in the ***Journal of the American Society of Nephrology***.

Researchers followed more than 120,000 patients requiring dialysis at 1,800 North American clinics for 4 years, 4% of whom were taking digoxin for concomitant heart disease. They found that the risk of death was 28% greater among patients taking digoxin vs. those not using the drug. Furthermore, researchers found that the risk of death was dose dependent, and patients taking higher doses of digoxin were more likely to die prematurely. Study authors noted that because the results were based on a surveillance study, more research is needed to determine what changes may be needed when treating patients on dialysis with digoxin.

GTx's Ostarine (GTx-024, formerly MK-2866) – moves further in development

GTx said it will meet with the FDA this summer to plan further development of Ostarine for preventing muscle loss in postmenopausal women. Results of a clinical trial including 88 postmenopausal women randomized to receive 3 mg Ostarine with MK-3984, another selective androgen receptor modulator, or placebo for 12 weeks showed that Ostarine met key study endpoints.

Imaging:

1. MRI – can predict outcomes in AFib patients non-invasively

A retrospective, cross-sectional, 65-patient study by researchers at the University of Utah Hospital found that delayed-enhancement MRI and echocardiography could differentiate between paroxysmal and persistent atrial fibrillation. Of the 55 patients included in the final analysis, 44% had paroxysmal and 56% had persistent AFib.

2. CV MR – can predict future CV events

A retrospective, 70-patient study found that CV magnetic resonance imaging could be used to characterize the tissue of an infarct core and the border zone, and the results correlated with future CV events in ischemic cardiomyopathy patients. The 29 patients (41%) who had CV events had a larger infarct border zone. A sub-analysis of the medical management and revascularized patients with CV events found the medically managed patients had a larger border zone, although there was no difference between border and core zones in the revascularization group ($p<0.05$).

JOHNSON & JOHNSON – increasing its push in diabetes with 2 acquisitions

J&J is buying Sweden's Diamyd Medical AB, which has a late-stage drug for Type 1 diabetes, and J&J licensed exclusive worldwide rights to several potential Type 2 diabetes drugs still in preclinical development from Metabolex. J&J also has its own diabetes drug in development, canagliflozin, (an SGLT-2 inhibitor).

MAP PHARMACEUTICALS' Levadex (dihydroergotamine mesylate) – positive headache data reported

This inhaled form of an IV migraine treatment was effective compared with placebo in a Phase III clinical trial in 771 patients with moderate-to-severe migraine pain. Researchers presented the results at the American Headache Society meeting in Los Angeles and said that Levadex was effective both when taken at headache onset and as late as 8 hours after the start of a migraine. A second analysis showed that Levadex was well tolerated by patients with asthma, with no significant differences in adverse effects seen among asthmatics vs. patients without asthma.

Melanoma – cases to almost double in next 9 years

This year Datamonitor is predicting 138,000 new cases of melanoma will be diagnosed, with that increasing to 227,000 new cases in 2019. Tom Gray, a senior healthcare analyst at Datamonitor, said, "There is a real opportunity for drug developers willing to invest in this market. A significant unmet need remains for more effective drugs, which makes melanoma a popular R&D target. While this has yet to translate into novel, effective therapies, there are several promising candidates in late-phase development that could change the face of melanoma treatment." He pointed to 11 products currently in Phase III development, calling Bristol-Myers Squibb's ipilimumab and Plexxikon/Roche's PLX-4032 the most promising. Genomics is also increasingly being used in melanoma studies to help identify patients who will respond. For example:

- PLX-4032 is being targeted at patients with V600E BRAF mutations.
- GSK's astuprotimut-r is targeted at patients with tumors overexpressing MAGE-A3.
- Novartis's Tasigna (nilotinib) is aimed at patients with c-kit mutations.

MOLECULAR INSIGHT's Azedra/Ultratrace (iobenguane I-131, I-131-MIBG) – positive Phase IIa data in neuroblastoma

Researchers presented data at the Advances in Neuroblastoma Research (ANR) conference in Stockholm, Sweden, showing that doses of 12-18 millicurie/kg were effective and well tolerated. The company plans to start a ***pivotal*** Phase II study under a Special Protocol Assessment (SPA) with the FDA.

NOVO NORDISK's Victoza (liraglutide) – to be tested as weight loss drug

A Phase III trial of Victoza as a treatment for obesity has been reinitiated now that the company has FDA approval for the drug in Type 2 diabetes. Novo plans to start enrolling >5,000

patients in 1H11 in a study comparing a fixed-ratio combination of both (a) insulin degludec + Victoza and (b) once-weekly liraglutide.

In addition, Novo said it will have a strategy in 2011 for development of semaglutide (a once-weekly GLP-1) and once-weekly liraglutide.

NYMOX PHARMACEUTICAL's NX-1207 – positive long-term results

The company reported positive long-term results, showing sustained benefit over time with this intraprostatic injection, which is administered in a urologist's office. With 48-60 months of follow-up, benign prostate hyperplasia (BPH) patients in Study NX02-0014 had no significant drug safety problems. The study, which includes results from all currently available patients, also found that:

- >37% of patients who received NX-1207 2.5 mg required no surgical treatments and were on no medications for their BPH. These patients had a mean improvement at 48-60 months of 10.1 points in their symptom scores. In comparison, only 2 patients in the control did not require any additional BPH treatments.
- With the NX-1207 2.5 mg dose, patients showed statistically significant improvement from baseline ($p<0.001$).

In previous multicenter U.S. trials, NX-1207, which is currently in Phase III trials, produced improvements in the BPH symptom score about twice that seen with currently approved BPH drugs and did so without the side effects commonly associated with those drugs, such as sexual dysfunction, blood pressure changes, and other adverse reactions.

PFIZER – suspended trials of tanezumab

On June 23, 2010, just days after reporting positive – but not impressive – data at the European League Against Rheumatism meeting in Rome on this nerve growth factor therapy for osteoarthritis (OA), Pfizer halted the entire worldwide tanezumab program at the request of the FDA due to reports of a "small number" of patients experiencing more severe osteoarthritis leading to joint replacement surgery. All of the joint replacements occurred in patients with OA; none occurred in the non-OA patients on tanezumab.

The clinical hold means no new patients will be enrolled in trials, and dosing will be stopped for osteoarthritis patients in all trials, not just those in the OA studies.

There was no hint of this side effect in the Phase III tanezumab data in osteoporosis that were presented at the European League Against Rheumatism. About 10% of those patients experienced "abnormal peripheral sensations," including some neuropathy, and 3%-5% had paresthesia, but there were no reports of joint surgery.

The FDA asked Pfizer to immediately give the Agency its assessment of the potential implications of this finding on other ongoing clinical studies of tanezumab. Tanezumab is being tested in cancer pain, interstitial cystitis, chronic low back pain, and diabetic neuropathy.

What are the possible explanations for the total joint replacement excess with tanezumab? It isn't clear who made the decision to do joint replacement surgery on these patients – but almost certainly it was an orthopedic surgeon, not the rheumatologist, so why was the patient referred to the orthopedic surgeon?

1. There could have been a mismatch in baseline OA seriousness. If more patients with very severe OA were enrolled in the tanezumab arm, that might explain why more tanezumab patients had joint replacement surgery.
2. It is possible patients were enrolled who were too on the edge for needing joint replacement surgery, perhaps even outside the trial guidelines. But then there should have been a balance between drug and placebo.
3. Maybe the joint replacements were in the ~30% of tanezumab patients who discontinued the trial for lack of efficacy, which might explain why they didn't show up as a serious adverse event. The problem with this explanation is that, again, there should have been a balance between drug and placebo.
4. Perhaps patients felt so good on tanezumab that they over-used the joint, worsening or destroying the joint – e.g., the "indomethacin hip." However, the efficacy of tanezumab just doesn't look sufficiently dramatic to result in this degree of over-use.
5. Maybe tanezumab drug causes excessive wear and tear on joints by degrading or destabilizing bone or cartilage. There is almost a doubling of arthralgia and extremity pain with 20 mg tanezumab vs. placebo, but, still, no signal of side effects severe enough to warrant joint replacement. This is the most concerning possibility.

What does this mean for the outlook for tanezumab approvals? That won't be clear until more is known about the joint replacement patients.

- The FDA is going to want to know what type of monitoring Pfizer is doing or going to do in cancer and neuropathic pain trials to be sure that this drug isn't causing joint damage, which will complicate those trials.
- This doesn't change the fact that neuropathic pain indications are more complicated to obtain in the U.S. than Europe. European regulators lump different types of neuropathic pain together, but the FDA requires proof (2 trials) in each type: diabetic peripheral neuropathy (DPNP), post-herpetic neuropathy (PHN), post-stroke neuropathy. Yet, the FDA may now make these trials more difficult with additional monitoring.

- The outlook in OA, in particular, is now questionable. If Pfizer can't market tanezumab as better than naproxen, it may not go ahead with the OA indication.
- In cancer pain, it doesn't look as if tanezumab is likely to have sufficient efficacy.

PFIZER's Mylotarg (gemtuzumab) – postmarketing withdrawal

Mylotarg has been withdrawn from the market at the request of the FDA after postmarket clinical trials showed no increased survival in patients with acute myeloid leukemia (AML) and an increased death rate among those being treated with the drug. Mylotarg was approved under the accelerated approval program in 2000 for patients older than age 60 with recurrent AML who were not candidates for other chemotherapy. Clinical studies at the time showed that Mylotarg was associated with liver veno-occlusive disease, and during the postmarket trial the rate of this fatal disorder increased.

QUINCY BIOSCIENCE's Prevagen (apoaequorin) – early data promising

Interim results from a 3-month, randomized, double-blind, placebo-controlled study showed statistically significant improvement with Prevagen over placebo at Day 60 in terms of spatial working memory and executive function in 35 generally healthy adults reporting memory concerns at baseline. Patients getting Prevagen (a calcium-binding protein derived from a jellyfish species) had a 14% reduction in the number of total errors from baseline. The company also is looking at several health conditions that are believed to be the result of disruptions in calcium homeostasis and intends to study the effect of Prevagen in these conditions.

SANOFI-AVENTIS's Lantus (insulin glargine) – cancer risk reported

German researchers reported in the online version of ***Diabetes Care*** that diabetics taking ≥0.3 IU/kg/day of Lantus had an increase in incident cancers. The retrospective study included 1,340 patients. ***Bloomberg News*** reported that Sanofi officials said the current study was too small to adequately detect an increased cancer risk, and experts at the American Diabetes Association meeting also disputed the finding, saying it wasn't supported by other studies.

SANOFI-AVENTIS/METABOLEX – licensing diabetes treatment from Metabolex

Sanofi will pay up to $375 million for rights to Metabolex's experimental diabetes treatment, MBX-2982, a GPR-119 agonist currently in mid-stage development. Metabolex will receive royalties on revenue from the drug and related therapies. ***Bloomberg News*** reports that the experimental drug is designed to boost production of both insulin and the hormone GLP-1.

FDA NEWS

CDRH to unveil 510(k) reform soon

Dr. Jeffrey Shuren, director of the FDA's Center for Devices and Radiological Health (CDRH), told a town hall meeting in Massachusetts that the FDA's report on its internal review of the 510(k) process will be completed and released within a few weeks. The FDA plans to seek public comments before implementing any changes. While Dr. Shuren hasn't released any details on what reforms will be in the final report, he insisted there are no plans to eliminate the 510(k) program, and he said that some companies applying for 510(k) clearance will be asked to submit more clinical data than in the past.

Asked if the Obama administration is pushing for stricter oversight of medical devices, Dr. Shuren said, "I have had absolutely no pressure or pushback" from the administration or from FDA Commissioner Dr. Margaret Hamburg.

Dr. Shuren added that one message the FDA has gotten from industry is: "The FDA needs to provide industry with clear, predictable pathways to approval and clearance. We hear you. We agree. And we're on it. Providing clear, predictable pathways to market will also help foster innovation, which is the other theme we've been hearing. We agree with you on this front, as well."

One more town hall meeting is scheduled this year: October in Los Angeles.

Expiration date reminder

The FDA says consumers should abide by the expiration date pharmacists list on the label of prescription medications. Many states require the expiration date to be no more than 1 year after the date the prescription is sold, and while many drugs stored under the correct conditions may retain potency long after the manufacturer's expiration date, the FDA urges purchasers to use the expiration date on the label. Ilisa Bernstein, the FDA's Director of Pharmacy Affairs, warned that there may not be data for a particular drug that ensures it is safe and effective beyond the date listed.

FDA auditing U.S. trial sites more than OUS sites

A report by the U.S. Department of Health and Human Services (HHS) found that FDA auditors are 16 times more likely to inspect domestic sites of clinical trials than foreign sites. "As sponsors increase the number of foreign clinical trials in support of FDA marketing applications, the Agency's current method of using inspections to ensure human subject

protections and data validity is becoming increasingly strained," wrote HHS Inspector General Daniel Levinson.

Infusion pumps

CDRH director Dr. Jeffrey Shuren said the FDA is collaborating with the University of Pennsylvania on open-source software for external infusion pumps that manufacturers can build on or use to benchmark their own products. He also said, "We've offered to perform diagnostics on infusion pump software at any stage of development – even before the device lands at our doorstep."

Orphan drug research urged

The FDA is urging several companies, including Roche, Johnson & Johnson, and Biogen Idec, to investigate orphan drugs for possible use in rare disorders. The FDA published a list of 235 existing agents that are already approved for other uses and is urging additional research with them. Director of the FDA's Office of Orphan Products Development, Dr. Tim Cote, said, "Large pharmaceutical companies are not as engaged as we'd like to see them be." A recent incentive program has failed to encourage additional research with these agents.

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Upcoming FDA Advisory Committees of Interest ***(items in red are new since last week)***

Date	Topic	Committee
June 28 **Cancelled**	**Lux's voclosporin** for the treatment of eye infections	The FDA said the meeting was cancelled to allow time for the resolution of several outstanding issues.
July 13-14	**GlaxoSmithKline's Avandia** (rosiglitazone) cardiovascular safety – and to a lesser extent the safety of **Takeda's Actos** (pioglitazone)	Joint meeting of the Endocrinologic and Metabolic Drugs Advisory Committee ***and*** the Drug Safety and Risk Management Advisory Committee
July 15	**Vivus's diet drug Qnexa** (phentermine + topiramate)	Endocrinologic and Metabolic Drugs Advisory Committee
July 19-20	**Oversight of laboratory-developed tests**, especially genetic tests	Public meeting
July 20	**Roche/Genentech's Avastin** (bevacizumab) – two supplemental BLAs for naïve metastatic HER2-negative breast cancer	Oncologic Drugs Advisory Committee (ODAC)
July 22-23	**REMS for long-acting opioids**	Joint meeting of the Anesthetic and Life Support Drugs Advisory Committee ***and*** the Drug Safety and Risk Management Advisory Committee
July 27-28	Meeting to obtain input on issues and challenges associated with the development and implementation of risk evaluation and mitigation strategies (**REMS**)	Public hearing
July 28	**AstraZeneca's Brilinta** (ticagrelor)	Cardiovascular and Renal Drugs Advisory Committee
July 30	**Glaukos's iStent Trabecular Micro-Bypass Stent** for treating open-angle glaucoma during cataract surgery	Ophthalmic Devices Advisory Committee
August 20	**Jazz Pharmaceuticals' Xyrem** (sodium oxybate, JZP-6) for fibromyalgia	Arthritis Advisory Committee joint meeting with the Drug Safety and Risk Management Advisory Committee
August 26	**Mela Sciences' MelaFind**, an optical device for melanoma detection	General and Plastic Surgery Devices Advisory Committee
September 17 (not confirmed)	**Boehringer Ingelheim's Pradaxa** (dabigatran)	Cardiovascular and Renal Drugs Advisory Committee