TRENDS-in-MEDICINE

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by Lynne Peterson

Quick Takes

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

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NOTE: Subscribe to ***Trends-in-Medicine*** for coverage of the **International Liver Congress** of the European Association for the Study of the Liver (EASL) in Amsterdam.

SHORT TAKES

- **ARCA BIOPHARMA's Gencaro (bucindolol)** – The company said a 200-patient clinical trial will be conducted in partnership with **Medtronic** to see if this investigational drug can prevent atrial fibrillation. Medtronic will provide implanted heart rhythm devices. In 2009 the FDA rejected Gencaro as a treatment for heart failure, issuing a complete response letter that said a large (3,000-patient) clinical trial would be needed prior to approval.

- **Autism** – The National Institute of Mental Health (NIMH) is giving the University of California, Los Angeles, $9 million to lead an effort to find effective drugs to treat autism. UCLA will form a collaborative network of researchers from other academic centers to try to identify promising new and older drug compounds quickly and to run early tests to see if they warrant further investment.

- **Bisphosphonates** – A study presented at the British Society for Rheumatology meeting found that bisphosphonates reduced the need for repeat joint replacement surgery by 40% vs. placebo. With 2.6 years of follow-up, revision surgery was required by 4.36% of patients not on a bisphosphonate vs. 1.88% of bisphosphonate users.

- **GALAPAGOS' GLPG-1790** – The company said that laboratory tests of this agent showed high activity against triple-negative breast cancer, and human trials will begin within a year.

- **HORIZON DISCOVERY's HD-001** – Horizon and **AstraZeneca** formed an exclusive collaboration and license agreement to investigate this kinase inhibitor program, which is in early development.

- **INSPIREMD's MGuard Embolic Protection Stent** – The company said the FDA granted investigational device exemption (IDE) approval for a trial in 1,114 STEMI patients in the U.S. and Europe.

- **Melanoma** – In a study published in the ***Journal of Virology***, researchers from Yale University School of Medicine demonstrated that the vesicular stomatitis virus (VSV) can find, infect, and kill human melanoma cells, both *in vitro* and in animals without really infecting non-cancerous cells. *If the data hold up in humans, this could be a promising new approach to melanoma.*

- **MERCK's lambrolizumab (MK-3475)**, a PD-1 inhibitor, was granted Breakthrough Status by the FDA to treat advanced melanoma.

- **NOVARTIS** – The U.S. Justice Department filed a lawsuit accusing Novartis of paying kickbacks in the form of rebates and discounts to pharmacists to get them to switch patients to **Myfortic** (mycophenolic acid), an immunosuppressant for transplant patients. Novartis was already under a five-year Corporate Integrity Agreement (CIA) that settled charges the company improperly promoted its **Trileptal** (oxcarbazepine) epilepsy drug and other medications. Novartis reportedly plans to dispute the new charges.

- **OMEROS' OMS-721** – The company submitted an application to the FDA seeking orphan drug designation for this investigational subcutaneous injectable treatment for atypical hemolytic uremic syndrome. Clinical trials are expected to start in summer 2013.

- **PFIZER's Celebrex (celecoxib)** – The company said this painkiller met the primary and secondary endpoints in a 6-week Phase IV safety trial in juvenile rheumatoid arthritis, showing no effect on either systolic or diastolic blood pressure vs. naproxen.

- **ROCHE's Actemra/RoActemra (tocilizumab)** – Data presented at the British Society for Rheumatology meeting from the ongoing, 2-year, double-blind, 188-patient CHERISH trial of Actemra in polyarticular juvenile idiopathic arthritis (JIA) found that this anti-IL-6 led to substantial and prolonged responses, with 25.6% of Actemra patients vs. 48.1% of placebo patients experiencing a disease flare-up (p=0.0024).

- **SANOFI/GENZYME's Aubagio (teriflunomide)** – The company said the 2-year Phase III TOPIC trial found that patients diagnosed with clinically isolated syndrome (CIS) after experiencing a first multiple sclerosis-like attack who took Aubagio were significantly less likely to convert to definite multiple sclerosis (have a second attack that means a diagnosis of MS). The conversion rate was reduced by 37% with Aubagio 7 mg/day and by 43% with 14 mg/day vs. placebo.

- **THERAVANCE** plans to split into two separate and publicly traded companies – Theravance Biopharma and Royalty Management Co., a joint venture with **GlaxoSmithKline** on respiratory drugs, including Breo Ellipta (fluticasone furoate/vilanterol) for chronic obstructive pulmonary disease (COPD).

- **XENON PHARMACEUTICALS and TEVA's XEN-402**, an investigational treatment for pain associated with erythromelalgia, a rare condition that can lead to attacks of severe burning pain in the hands and feet, was granted orphan drug status.

NEWS IN BRIEF

AMGEN's Kineret (anakinra) – in the eye?

An eye drop formulation of this arthritis drug may be an effective dry eye treatment. A 12-week Phase I/II proof-of-concept study published in ***JAMA Ophthalmology*** found that eye drops with this interleukin-1 receptor antagonist (2.5% or 5%) were safe and significantly reduced both signs and symptoms of dry eye vs. **Allergan's Refresh Liquigel** (1% carboxymethylcellulose).

Phase I/II Results with Kineret in Dry Eye

Measurement	Kineret 2.5%	Kineret 5%	Refresh Liquigel
Primary endpoint #1: Reduction in corneal staining vs. baseline	46% (p<0.001)	17% (Nss)	19%
Primary endpoint #2: Complete bilateral	29% (p=0.03)	7% (Nss)	7%
Primary endpoint #3: Dry eye symptom reduction	30% (p=0.02)	35% (p=0.01)	5%

All three primary endpoints – reduction in corneal fluorescein staining (CFS), the proportion of patients in whom the CFS cleared from both eyes within 3 minutes, and reduction in symptoms as measured by the Ocular Surface Disease Index – were met at the lower dose, but only symptom reduction was significant for the high dose. *The question is why the lower dose was more effective than the higher dose.*

BIOGEN IDEC's Tecfidera (dimethyl fumarate, BG-12) – indirect association with PML

Just a month after gaining FDA approval, a cloud has formed over this oral multiple sclerosis drug related to **Fumaderm** (fumaric acid esters), an oral psoriasis treatment from Germany that Biogen got in 2006 with its purchase of **Fumapharm**. The active agent in Fumaderm was reformulated into Tecfidera, but Fumaderm continued to be sold in Europe.

Case reports published in the ***New England Journal of Medicine* (*NEJM*)** described four cases of PML (progressive multifocal leukoencephalopathy), a catastrophic brain disease, in Europe:

- A 74-year-old German man who had taken Fumaderm for three years for psoriasis. Neurological symptoms consistent with PML developed in 2010.

- A Fumaderm patient who had also been taking methotrexate and steroids.

- A patient who, in addition to Fumaderm, had been taking Genentech's Raptiva (efalizumab), which also has been linked to PML.

- A 42-year-old Dutch woman who had taken a compounded version of fumarate, **Psorinovo**, for five years. This patient developed neurological symptoms (e.g., right-side hemiparesis in 2012) about six months before the PML was diagnosed in 2012.

Remember that it was PML that caused Biogen's **Tysabri** (natalizumab) to be taken off the market and only allowed back with a very, very strict risk evaluation and mitigation strategy (REMS) that basically limits use to JC virus-negative patients. Apparently, Biogen had disclosed at least some of the cases to the FDA prior to Tecfidera's approval.

In its response in the ***NEJM***, Biogen emphasized that the PML patients had not been taking fumarate for MS, though why that is important is uncertain. What matters is that there is a link between the active ingredient and PML.

The FDA is unlikely to restrict use of Tecfidera in some way until or unless there are cases of PML in Tecfidera patients, but it would not be surprising to see the FDA issue a safety advisory about this.

Breast cancer – a microRNA approach

A study led by researchers at Ohio State University Comprehensive Cancer Center – published in the ***Journal of Experimental Medicine*** – found that a new agent, AS-1411 (a G-rich aptamer), may reverse resistance to fulvestrant, improve effectiveness of other oncology drugs, and slow breast cancer growth and metastasis by changing the levels of cancer-associated microRNAs. AS-1411 works by inhibiting nucleolin.

Among the key findings in the study were:

- Nucleolin is present at abnormally high levels in breast cancer cells.
- AS-1411 reduces nucleolin levels and inhibits the processing of certain cancer-associated microRNAs whose overexpression in breast cancer is associated with drug resistance and aggressiveness.
- AS-1411 affects breast cancer cell motility and invasiveness by reducing the expression of several genes targeted by nucleolin-related microRNAs (e.g., PTEN).
- Impairing nucleolin in fulvestrant-resistant breast cancer cells restores sensitivity to the drug, suggesting that agents targeting nucleolin can improve the effectiveness of conventional anti-cancer agents.

Electronic health records – confusion over rules

A survey by Stoltenberg Consulting found that the biggest barrier to achieving meaningful use of electronic health records (EHRs) is confusion over the meaningful-use rules. However, competing health information technology efforts and lack of IT workers, funding, and other resources were also cited.

The Office of the National Coordinator for Health Information Technology revoked the certification of two EHR systems from the same company: **EHRMagic's EHRMagic-Ambulatory** and **EHRMagic-Inpatient**. What do doctors and hospitals do who have these systems? Get a new one, obviously. *This could slow down adoption of EHRs or at least cause doctors to stick with the big-name companies.*

HIV vaccine – trial halted for futility

The National Institute of Allergy and Infectious Diseases (NIAID) halted a 2,504-person Phase IIb trial, the HVTN-505 study, of the investigational vaccine for futility. The independent safety monitoring board found it did not reduce the virus in recipients' blood, with 41 people on the vaccine getting infected vs. 30 on placebo. In addition, the vaccine was associated with a numerical (but not statistically significant) increase in the likelihood of contracting HIV vs. placebo (27 vs. 21 participants).

mTOT modulators – a promising new approach to Type 2 diabetes

A multicenter, proof-of-concept, 258-patient, 12-week Phase IIb study, published in ***Clinical Pharmacology & Therapeutics***, found that treatment with **Metabolic Solutions Development Company's MSDC-0160** effectively lowered glucose levels in Type 2 diabetics. This mitochondrial target of thiazolidinediones (mTOT) modulator was effective without many of the side effects typically seen with peroxisome-proliferator-activated receptor (PPAR)-γ inhibitors such as **Takeda's Actos** (pioglitazone). The trial compared three doses of MSDC-0160 (50 mg, 100 mg, and 150 mg) to Actos and to placebo. Most patients in all arms also took metformin.

MSDC-0160 Phase IIb Results

Measurement	MSDC-0160 50 mg	MSDC-0160 100 mg	MSDC-0160 150 mg	Placebo	Actos 45 mg
HbA_{1c} change	N/A	– 18.4 mg/dL	– 28.9 mg/dL	increased	– 31 mg/dL
Edema	11.8%	13.0%	5.7%	11.4%	8.5%
Hemoglobin	---	---	---	---	Biggest decrease
Body weight change	Increased	Increased	Increased	Decreased	Increased more than with MSDC-0160
Increase in waist circumference	No	No	No	---	Yes

Oncologists – complaining about drug prices

In an article published in ***Blood***, the journal of the American Society of Hematology, more than 100 hematologists/oncologists demanded that pharmaceutical companies reduce the prices of their medications. Noting that 11 of the 12 cancer medications approved by the FDA last year cost more than $100,000/year, the doctors acknowledged that pharmas need to make a profit but said oncology drugs should be priced "affordably."

The doctors wrote, "We believe the unsustainable drug prices in [chronic myeloid leukemia] and cancer may be causing harm to patients…Advocating for lower drug prices is a necessity to save the lives of patients who cannot afford them."

Hagop Kantarjian, MD, chairman of the Leukemia Department at MD Anderson Cancer Center and an author of the article, said, "We believe that lowering the prices of CML drugs might improve accessibility to treatment and increase treatment adherence."

Renal denervation – guidelines issued

The European Society of Cardiology (ESC) and the European Association of Percutaneous Cardiovascular Interventions (EAPCI) issued an expert consensus document on catheter-based renal denervation that offers guidance on patient selection, site selection, efficacy, safety, limitations, and potential new indications for referring physicians, interventionalists, and healthcare providers. The guidance was published in the ***European Heart Journal***.

The ESC said it hopes insurance companies and healthcare providers will decide to pay only sites and cover patients that are in accordance with the guidance.

The paper says that renal denervation is currently indicated for blood pressure control in patients with resistant hypertension (systolic blood pressure ≥160 mmHg or ≥150 mmHg in Type 2 diabetics) despite treatment with ≥3 antihypertensive drugs of different types and in adequate doses, including one diuretic as well as lifestyle modification.

The guidance also:

- Recommends that sites be specialized in the management of hypertension.
- Suggests that at least one hypertension expert at each site should be involved in treatment and screening.
- Says interventions should be performed by interventional cardiologists or angiologists with training in percutaneous renal artery access.
- Recommends that sites perform >25 renal artery denervations annually to ensure they have the required experience.

Long-term follow-up data are needed.

ROCHE – reorganizing Applied Science business

Although Roche claims to remain committed to the life-science business, it is making major changes to its Applied Science business, including:

- The Applied Science Business Area is being dissolved as of the end of 2013. Its portfolio of products will be integrated within Roche's other Diagnostics Business Areas.
- In the sequencing area, Roche is:
  - Returning the ISFET project for the development of a semiconductor-based sequencing system to **DNA Electronics**, saying it is unlikely to be a disruptive technology at launch.
  - Ending its partnership with **IBM** for the development of a nanopore-based sequencing platform, citing high technical risks.
- Polymerase chain reaction technology (PCR) and nucleic acid product lines (NAP) will be managed by Roche Molecular Diagnostics.
- The Custom Biotech portfolio, which includes platforms and reagents, will move to Roche Professional Diagnostics.
- A dedicated unit will be established to focus solely on sequencing and will be tasked with implementing a sequencing strategy from life-science research to clinical diagnostics, exploring internal and external opportunities to provide customers with differentiated products, and managing Roche's existing sequencing business.

SANOFI/GENZYME's Renagel (sevelamer) – no CV benefit in CKD

A single-center, randomized, 40-week, 12-patient U.K. study published in the ***Journal of the American Society of Nephrology*** found that cardiovascular (CV) outcomes (left ventricular mass, left ventricular function, or arterial stiffness) were not improved in Stage III chronic kidney disease (CKD) patients given this phosphate binder vs. placebo.

However, adherence in the study was poor. In an accompanying editorial, Rajiv Agarwal, MD, of Indiana University wrote, "This study does not answer the question of whether treatment of hyperphosphatemia benefits the cardiovascular system."

Statins – lots of excuses for not filling prescriptions

Why don't people fill their statin prescriptions? In a 98-patient telephone survey – conducted by **Kaiser Permanente**, funded by **Merck**, and published in the ***American Journal of Managed Care*** – 74.5% of people who were given a new prescription for statins did not fill it in the next 2 weeks. The reasons for not filling the prescriptions were:

- 53% said it was because of concerns about side effects.
- Two-thirds said it was because of general concerns about statins.
- 40% said the medication was unnecessary.
- 35% did not consider high cholesterol life-threatening.
- A third said they were taking non-prescription medications (e.g., over-the-counter supplements) instead.
- 63% said they decided to make changes to their lifestyle (diet and exercise) first.
- 12% cited cost.

REGULATORY NEWS

New HIT Policy Workgroup

The Department of Health and Human Services (HHS) and the Federal Communications Commission created a new advisory panel, the FDA Safety and Innovation Act Workgroup, which is charged with promoting patient safety, fostering innovation, and streamlining the regulatory environment. The group, which will write a report on strategies and recommendations for a risk-based regulatory framework for HIT including medical mobile applications, will advise the FDA, the Federal Communications Commission, and the Office of the National Coordinator for Health Information Technology. The panel's first meeting is April 29, 2013.

Oversight of compounding pharmacies – and what it means for Avastin

The Senate Health, Education, Labor, and Pensions (HELP) Committee finally issued the draft legislation giving the FDA some (actually a lot of) authority over compounding pharmacies. Among the key provisions are:

- A clear boundary is drawn between traditional compounders and compounding manufacturers, and each is defined.
- Compounded drugs are new drugs subject to FDA oversight.
- Compounding pharmacies must:
  - Register with the FDA.
  - Divulge what products they have made.
  - Make products under a pharmacist's oversight and in compliance with Good Manufacturing Practices (GMP).
  - Investigate and report adverse events.
  - Label products as compounded.
  - Pay an annual fee.
- States will continue to oversee traditional compounders.

What does this mean for compounding of ***Roche/Genentech's Avastin*** *(bevacizumab) for age-related macular degeneration (AMD)?* It clearly puts Avastin in the compounding manufacturer camp. The definition of a compounding manufacturer is "an entity that compounds a sterile drug prior to or without receiving a prescription and introduces such drug into interstate commerce, with the exception that interstate shipment within a hospital system will not cause a hospital pharmacy to be considered a compounding manufacturer. Any entity that pools sterile products, or that repackages sterile, single-use, preservative-free vials is also a compounding manufacturer."

The committee's statements also muddied the waters a little with respect to what this means for Avastin. In one instance, the committee said: "The draft legislation allows FDA to identify categories of drugs that currently cannot be safely compounded…[and places] prohibitions on wholesale distribution of compounded products."

In another statement, the legislation appears to specifically prohibit compounding of biologics: "The draft legislation …prohibits compounding of certain drug products, including those identified by regulation as being demonstrably difficult to compound (such as complex dosage forms and **biologics**), marketed FDA-approved drugs that are not in shortage, variations of marketed FDA-approved drugs unless they fulfill a specific patient need, or products subject to certain risk evaluation and management strategies unless the compounder utilizes comparable safety controls. Wholesale distribution of compounded products is also not permitted."

So, it is still not clear whether compounding manufacturers will be allowed to compound Avastin for retina specialists and AMD patients. Hopefully, the committee will clarify this soon. A formal request for clarification has been made.

FDA approvals/clearances

- **ASPECT IMAGING's M2**, a compact MRI scanner, was cleared for use in wrist imaging.
- **CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 Assay**, a test for H7N9 flu, received an emergency use authorization from the FDA. The test will run on **Applied Biosystems' 7500 Fast Dx Real-Time PCR** platform.
- **ECHOSENS' FibroScan** – The company received 510(k) clearance for this non-invasive ultrasound elastography system for determining liver fibrosis.
- **GE HEALTHCARE's MR therapy planning suite**, a 1.5-tesla geometry-embracing method (GEM) of delivering large field-of-view and high-resolution images of the neck and head when used with the company's **Optima 450w GEM MR** technology during radiation treatment planning, received 510(k) clearance.
- **NOVARTIS/ALCON's Simbrinza (brinzolamide + brimonidine tartrate)** was approved to treat open-angle glaucoma and ocular hypertension. It is the first fixed-dose combination glaucoma therapy without a beta blocker.
- **OLYMPUS MEDICAL's Articulating HD 3D system**, which is used to help surgeons perform laparoscopic procedures more efficiently and accurately, was granted 510(k) clearance.
- **SOUTHERN SPINE's StabiLink MIS Spinal Fixation System** for lumbar fusion surgeries was cleared for use.
- **WARNER CHILCOTT's Minastrin 24 FE**, an oral contraceptive, received FDA approval. However, the company does not plan a commercial launch this year.

FDA recalls/warnings

- **BALANCED SOLUTIONS COMPOUNDING PHARMACY** announced a voluntary recall of all of its sterile compounded products due to concerns about quality control processes and sterility.
- **CAREFUSION's Alaris PC** – A Class I recall was initiated after customers complained about communication problems with these infusion pumps.
- **COOK MEDICAL's Zilver PTX** – The company initiated a voluntary global recall of this paclitaxel-eluting peripheral stent after receiving 13 complaints that the delivery system tip separates.
- **EXCEL MEDICAL PRODUCTS**, which makes Class II hemostatic Y-connectors, received a warning letter that it is not in conformity with current GMP (cGMP).
- **GE HEALTHCARE's Giraffe incubator and Giraffe Omnibed** – The company initiated a voluntary, nationwide field correction action for these products, which was then upgraded to a Class I recall.
- **HOSPIRA** recalled one lot of 0.9% sodium chloride injection USP 100 mL containers due to four separate reports of particulate contamination.
- **NORA APOTHECARY** issued a multi-state recall of all of its sterile compounded products due to lack of sterility assurance.

European regulatory news

- **New guidelines on anticoagulants.** The European Heart Rhythm Association (EHRA), of the European Society of Cardiology (ESC), issued a "practical guide" on the use of the new oral anticoagulants, which was published in the ***European Heart Journal***. Among the recommendations were:
  - New oral anticoagulants are preferable to warfarin for stroke prevention in atrial fibrillation patients.
  - Doctors should educate patients about the importance of adherence.

  The guidance also provides practical advice on how to handle 15 specific clinical scenarios as well as tips on how to improve patient compliance. While it does not say when or why patients should be switched from warfarin to an oral anticoagulant, it does advise how to make the switch safely once that decision is made.
- **PFIZER's Xeljanz (tofacitinib)** – The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) recommended against approval of this rheumatoid arthritis (RA) drug, saying it improved physical function and RA symptoms but failed to demonstrate a consistent reduction in disease activity and structural joint damage. CHMP also raised concerns about infections, gastrointestinal perforations, and carcinogenicity. Pfizer plans to appeal the recommendation.
- **ROCHE's Erivedge (vismodegib)** – CHMP recommended conditional approval of this treatment for symptomatic basal cell carcinoma and for locally advanced basal cell carcinoma patients ineligible for surgery or radiotherapy.
- **SANOFI PASTEUR's Hexyon/Hexcima** – This 6-in-1 vaccine combination of diphtheria, tetanus, pertussis, hepatitis B, polio, and influenza Type B received expanded approval from the European Commission for use in infants.

- **SOUTHERN SPINE's StabiLink MIS Spinal Fixation System** for lumbar fusion surgeries received a CE Mark.
- **VENTRIPOINT DIAGNOSTICS' VMS platform** got expanded approval, with CE Mark approval of the NRV application, a 2-D ultrasound imaging application that enables imaging of the right ventricle in patients with right heart conditions but no pulmonary hypertension or significant congenital heart defects.

Regulatory news from other countries

- ***Brazil*** is revising its procedures for appointing certification bodies for product conformity assessment and for setting new technical standards for testing laboratories as part of an effort to reform its GMP and to streamline market access for healthcare products and medical devices.
- ***New Zealand*** created an online portal for clinical trials that is accessible to physicians, researchers, and the general public. It will provide information about trials in that country, including who is eligible and how to participate.
- ***Russia.*** **ABBOTT**'s plan to buy **Petrovax** was rejected by the Commission on Foreign Investment.
- ***Taiwan*** issued new regulations, effective immediately, that are designed to expedite approval of imported drugs that have been available for ≥10 years in the U.S., the U.K, Switzerland, Sweden, Japan, Germany, France, Canada, Belgium, or Australia.

2013 FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
April 29	Discussion of general factors in **risk communication about FDA-regulated products**, including messaging in the context of competing communicators	FDA's Risk Communication Advisory Committee
April 29	**Shire's Vyvanse** (lisdexamfetamine dimesylate), sNDA for ADHD treatment in children	PDUFA date
April 29-30	Discussion of **medical device labeling standardization**, including an online labeling repository for in-home medical devices	FDA public workshop
April 30	Discussion of how to communicate effectively about the FDA's **adverse event reporting system** (AERS)	FDA's Risk Communication Advisory Committee
April 30	**Raptor Pharmaceutical's Procysbi** (cysteamine bitartrate delayed-release, RP-103) to treat nephropathic cystinosis	PDUFA date (extended from January 30, 2013)
April 30	**Titan Pharmaceuticals' Probuphine** (buprenorphine implant) for opioid dependence	PDUFA date
May 2	**Allergan's Juvéderm Voluma XC**, a facial filler with hyaluronic acid and lidocaine	FDA's General and Plastic Surgery Devices Advisory Committee
May 2	**Aveo and Astellas' Tivopath** (tivozanib) for advanced renal cell carcinoma	FDA's Oncologic Drugs Advisory Committee
May 3	Discussion of the controversy over the **appropriate use of electronic health records (EHRs)** without fraudulently increasing healthcare claims	Centers for Medicare and Medicaid Services (CMS) and the Office of the National Coordinator for Health Information Technology (ONC) public hearing
May 12	**GlaxoSmithKline** and **Theravance's Breo Ellipta** (fluticasone furoate + vilanterol) to treat chronic obstructive pulmonary disease (COPD)	PDUFA date
May 22	Possible **reclassification of pedicle screws** used in spinal fusion surgeries	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee
May 31	**Depomed's Sefelsa** (gabapentin extended-release), a hot-flash treatment (formerly known as Serada)	PDUFA date
June 5-6	**GlaxoSmithKline's Avandia** (rosiglitazone) – discussion of an independent readjudication by Duke University of the safety of this TZD in the RECORD trial	FDA's Endocrinologic and Metabolic Drugs Advisory Committee joint meeting with the Drug Safety and Risk Management Advisory Committee
June 20	**Dainippon Sumitomo Pharma/Sunovion Pharmaceuticals' Latuda** (lurasidone), a schizophrenia drug for use in treating bipolar disorder	PDUFA date
June 24-25	Discussion of the performance of **medical devices in women**	FDA public workshop
June 28	**Hisamitsu Pharmaceutical/Noven Pharmaceuticals' Pexeva** (paroxetine mesylate), a low-dose SSRI antidepressant to treat non-hormonal hot flashes in menopausal women	PDUFA date
July tba	**PET imaging** of brain beta-amyloid	CMS coverage decision expected
July 24	**SpinalMotion's Kineflex/C**, a metal-on-metal cervical artificial disc	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee
July 25	**SpinalMotion's Kineflex Lumbar Artificial Disc**, a metal-on-metal lumbar artificial disc	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee
July 28	**Aveo Oncology** and **Astellas Pharma's Tivopath** (tivozanib) to treat advanced renal cell carcinoma	PDUFA date
August 17	**ViiV Healthcare's dolutegravir** for HIV	PDUFA date
September tba	**Sanofi/Genzyme's Lemtrada** (alemtuzumab) for multiple sclerosis	PDUFA date
October tba	**Gilead Sciences' sofosbuvir** + interferon and ribavirin to treat hepatitis C, genotypes 1-4-5-6, without interferon to treat genotype 2/3 ***and/or*** **Johnson & Johnson's simeprevir** + interferon and ribavirin to treat hepatitis C, genotype 1	FDA's Antiviral Drugs Advisory Committee
October 2	**Lundbeck** and **Takeda's Brintellix** (vortioxetine), an antidepressant for major depressive disorder	PDUFA date
October 3	**Pfizer** and **Ligand Pharmaceuticals' Aprela** (bazedoxifene/conjugated estrogens) to treat menopausal symptoms and osteoporosis prevention	PDUFA date
October 19	**Actelion's Opsumit** (macitentan), a dual endothelin receptor antagonist to treat pulmonary arterial hypertension	PDUFA date
October 21	**AMAG Pharmaceuticals' Feraheme** (ferumoxytol) expanded indication	PDUFA date
October 28	**Neos Therapeutics' NT-0202** (extended-release tablet formulation of amphetamine polistirex) to treat ADHD	PDUFA date
December 18	**GlaxoSmithKline** and **Theravance's Anoro** (umeclidinium bromide + vilanterol) for COPD	PDUFA date