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…

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 **Cardiovascular Research Technologies (CRT)** meeting in Washington DC and the **American Academy of Dermatology** meeting in Miami FL.

SHORT TAKES

- **Alzheimer's disease –** Researchers from the University of Florida and Johns Hopkins University reported in ***The Journal of Neuroscience*** that they have developed a line of genetically altered mice that model the earliest stages of Alzheimer's disease (AD), which could help development of new drugs to treat AD.

- **AMARIN's Vascepa (icosapent ethyl) –** The company filed a supplemental new drug application (sNDA) with the FDA for approval to market this omega-3 fatty acid to adult patients with high triglycerides and mixed dyslipidemia.

- **AMGEN's Sensipar (cinacalcet) –** All three of the ongoing pediatric clinical trials of this calcium-sensing receptor agonist for hyperparathyroidism in patients age <18 with chronic kidney disease were halted after a 14-year-old patient in one of the trials died. The FDA has not yet determined whether Sensipar is to blame, but the trials are on hold until the death is investigated. The FDA also issued a reminder warning to healthcare professionals to monitor serum calcium levels in patients taking Sensipar.

- **AVEO PHARMACEUTICALS and ASTELLAS' Tivopath (tivozanib) –** The FDA's Oncologic Drugs Advisory Committee will review this oral, once-daily investigational tyrosine kinase inhibitor for advanced renal cell carcinoma on May 2, 2013.

- **Barrett's esophagus –** A study published in ***Cancer Prevention Research*** identified a series of microRNA expression signatures that may serve as biomarkers for early diagnosis of the progression of Barrett's esophagus into esophageal adenocarcinoma.

- **BAXTER's FEIBA NF –** The company submitted a biologics license application (BLA) supplement for this hemophilia drug that is nanofiltered and vapor heated – an anti-inhibitor coagulant complex treatment – to the FDA.

- **BOSTON SCIENTIFIC's Watchman –** A post hoc analysis of the PROTECT-AF trial, published in the ***Journal of the American College of Cardiology***, found that atrial fibrillation patients had "modestly" but significantly better quality of life – primarily an improvement in physical functioning – at one year with closure of their left atrial appendage (LAA) with Watchman than patients who took warfarin to prevent strokes. The results of the pivotal PREVAIL trial will be reported at the American College of Cardiology (ACC) meeting on March 9, 2013.

- **Breast cancer** – Researchers at Vanderbilt University reported in the ***Journal of the National Cancer Institute*** that they have identified a new genetic risk factor for breast cancer – APOBEC3 genes. A woman with a deletion in one of the two sets of genes she inherits from her parents has a 31% increased risk of breast cancer, and with deletions in both sets of genes, the risk goes up by 76%.

- **Cardiac resynchronization therapy + defibrillation (CRT-D)** – A new analysis of data from the MADIT-CRT trial suggested that these devices can benefit even mild heart failure patients with left ventricular ejection fraction (LVEF) >30%. Currently, the devices are indicated for patients with LVEF <30%, but in the analysis, patients with LVEF of >30% had a 44% risk reduction with CRT.

- **CEPTARIS THERAPEUTICS' mechlorethamine hydrochloride** – The company resubmitted its NDA for this investigational gel to treat early stage mycosis fungoides, a type of cutaneous T-cell lymphoma (CTCL). The FDA rejected the drug in May 2012, asking for more data.

- **DAINIPPON SUMITOMO PHARMA/SUNOVION PHARMACEUTICALS' Stedesa (eslicarbazepine acetate)** – The company resubmitted this investigational agent for managing partial onset seizures in epileptics, and the FDA accepted the submission. Three years ago, the FDA rejected Stedesa, saying additional data were needed, but the company said it now has more data. The drug is already approved in Europe as Zebinix.

- **DYNAVAX TECHNOLOGIES' Heplisav (1018 ISS and HBsAg)** – The FDA rejected this hepatitis B vaccine, issuing a complete response letter asking for an additional safety study in a broad patient population, but saying it is open to a more restricted approval based on the patients already studied. The company plans to meet with the FDA to discuss the path forward.

- **ELAN** – **Royalty Pharma** made an offer to buy Elan.

- **GLAXOSMITHKLINE's Pandemrix** – In a report published in the ***British Medical Journal***, the U.K.'s Health Protection Agency reported finding a link between this swine-flu vaccine and an increased risk of narcolepsy in British children. The researchers estimated that receiving the Pandemrix vaccine was associated with a 14- to 16-fold increase in the risk of developing narcolepsy, with an estimated risk of 1:50,000 doses. This finding follows similar findings in Finland and Sweden. The vaccine was not used in the U.S. and is being attributed to an adjuvant in the vaccine.

- **GLP-1 agonists and DPP4 inhibitors** – An analysis of FDA adverse event data, published in ***JAMA Internal Medicine***, found these drugs for Type 2 diabetes – e.g., **Merck's Januvia** (sitagliptin) and **Amylin's Byetta** (exenatide) – double the risk of acute pancreatitis, which in turn was linked to cancer and kidney failure. The researchers recommended that patients taking these drugs know the symptoms of pancreatitis (abdominal pain, nausea, and persistent vomiting) and seek treatment if those symptoms occur.

- **Gout** – A study published in the ***Journal of Clinical Pharmacology*** found that patients taking generic allopurinol long term for gout control are at increased risk for adverse events if they concomitantly use either colchicine or a statin.

- **Heart failure** – Spironolactone, an aldosterone inhibitor, missed one of two primary endpoints in the ALDO-DHF trial, published in the ***Journal of the American Medical Association (JAMA)***. In heart failure patients with preserved ejection fraction, at one year the drug significantly improved left ventricular diastolic function vs. placebo but did not improve maximal exercise capacity on cardiopulmonary exercise testing (peak VO2), and it failed to improve quality of life measures. On March 10, the results of the REMINDER trial of **Pfizer's Inspira** (eplerenone), another aldosterone inhibitor, in acute myocardial infarction (AMI) patients without heart failure will be reported at ACC.

- **Influenza** – Scientists in Australia and the U.K. discovered a neuraminidase inhibitor that could prevent the spread of multiple strains of flu by inhibiting how the virus works in the human body. Flu viruses bind to sugars in the cell and remove the sugars. Scientists at the science institute CSIRO said lab tests showed the drug stopped the virus from removing the sugars.

- **MACROGENICS' teplizumab** – A study published in ***Diabetes*** found that teplizumab, an anti-CD3 antibody, reduced the rate of beta-cell death in patients with new-onset Type 1 diabetes vs. patients with long-standing diabetes or no diabetes. *So, this drug, which failed in a Phase III Lilly trial 2.5 years ago, may have some life in it yet.*

- **MERCK KGAA's cilengitide** – This selective αvβ3/5 integrin inhibitor failed in the Phase III CENTRIC trial in newly diagnosed glioblastoma, with no significant improvement in overall survival from adding it to chemoradiotherapy [**Merck's Temodar** (temozolomide) + radiation]. The full results of the trial will be presented at the American Society of Clinical Oncology (ASCO) meeting in June 2013.

- **NEUROPACE's RNS System** – The FDA's Neurological Devices Advisory Committee voted 11-0 (with 2 abstentions) to recommend approval of this implantable neurological device designed to reduce the frequency of epileptic seizures.

- **ROCHE's Herceptin (trastuzumab)** – A study published in ***Cancer Research*** suggested that drugs targeting HER2 may be beneficial in more than just HER2-positive breast cancer. The researchers found that there are HER2+ clusters of breast cancer stem cells (CSCs) in women with otherwise HER2-negative breast cancer, and these CSCs may be sensitive to the targeted therapies. When the researchers gave Herceptin to HER2-negative mice, Herceptin blocked the tumors from growing – but only if the drug was given when the cancer first metastasized to the bone, not later.

- **ROCHE/GENENTECH and NOVARTIS' Xolair (omalizumab)** – A 323-patient, 3-month Phase III trial – published in the ***New England Journal of Medicine*** and presented at the American Academy of Allergy, Asthma, and Immunology (AAAAI) meeting – found that this asthma medication dose-dependently relieved itchiness in patients with chronic idiopathic urticaria (hives) for whom traditional antihistamines do not work. However, when the drug was discontinued, symptoms slowly returned, leading the researchers to suggest that duration of therapy may need to be longer.

- **TEVA/CEPHALON's Treanda (bendamustine)** – Adding Treanda to **Roche/Genentech's Rituxan** (rituximab) is better than the conventional regimen of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone + Rituxan) in patients with newly diagnosed indolent non-Hodgkin's lymphoma or mantle cell lymphoma. That was the finding of a study published in ***The Lancet***. With 45 months of follow-up, median progression-free survival (PFS) was significantly longer with Treanda + Rituxan than with R-CHOP (69.5 vs. 31.2 months, HR 0.58).

NEWS IN BRIEF

Bariatric surgery – a pair of studies

- A subanalysis of the STAMPEDE trial, published in ***Diabetes Care***, found that Roux-en-Y gastric-bypass surgery was better than either sleeve gastrectomy or optimal medical therapy in reducing HbA_{1C} and increasing insulin sensitivity and beta-cell function in diabetics. At 2 years, HbA_{1C} decreased to 6.7% with Roux-en-Y, 7.1% with sleeve gastrectomy, and 8.4% with medical therapy. Insulin sensitivity increased 2.7-fold with Roux-en-Y but didn't improve with the other therapies.

- A study published in ***JAMA*** found that having bariatric surgery at a "center of excellence" vs. another hospital did not result in significantly fewer complications (5.5% vs. 6.0%) or a lower reoperation rate (0.83% vs. 0.96%).

INTUITIVE SURGICAL's da Vinci – two surveys

- An online survey by ***MedPage Today*** found that 50% of respondents believe it is time to limit robotics in the surgical suite, 32% disagreed, and 18% were unsure.

- The FDA conducted its own hospital survey, asking surgeons about any complications they have seen with da Vinci, about their robotic training, and the surgeries for which the robots are best/least suited. The FDA conducted the survey to see if the adverse events being reported to the Agency are representative as a problem with the robots.

MERCK's Tredaptive (extended-release niacin + laropiprant) – raises myopathy risk

An analysis of the 25,673-patient HSP2-THRIVE study, published in the ***European Heart Journal***, found that this cholesterol medication raised the risk of muscle pain (myopathy) and weakness. Among the results at four years were:

- Muscle pain/weakness was significantly higher among Chinese patients (0.66% of Chinese patients vs. 0.12% with placebo and vs. 0.07% of European patients), a 10-fold increase by geography.

- Overall, Tredaptive patients had a significant, four-fold increased risk of myopathy vs. placebo.

- 25% of Tredaptive patients discontinued therapy vs. 17% of placebo patients, with rash, flushing, and gastrointestinal side effects the main reasons.

- Tredaptive patients were four times more likely to stop for skin-related adverse side effects vs. placebo and twice as likely to stop for gastrointestinal problems or diabetes-related problems.

The cardiovascular outcomes data from the trial will be presented on March 9, 2013, at ACC. In an accompanying editorial, Ulf Landmesser, MD, a Swiss cardiologist, wondered whether laropiprant "is really biologically inert with respect to atherosclerosis and thrombosis."

Prostate cancer – new viral discovery

Virginia Polytechnic Institute (VPI) researchers reported in the ***Journal of Virology*** that they identified a recombinant Newcastle disease virus that kills all kinds of prostate cancer cells, including hormone-resistant cells, but leaves normal cells unscathed. Newcastle disease virus kills chickens but does not harm humans. This oncolytic virus previously showed promising results in a number of human clinical trials in various cancers, but the treatment required multiple injections of large quantities of virus. The VPI researchers modified the virus' fusion protein, enabling the virus to enter the host cell but only with the help of a prostate-specific antigen, which minimizes the off-target effects.

RECKITT BENCKISER's Suboxone (buprenorphine) – FDA actions

- The FDA relaxed restrictions on the prescribing of this opioid addiction treatment, giving doctors and opioid treatment programs more flexibility in using it to wean patients off opiates.
- The FDA rejected Reckitt Benckiser's Citizen Petition that sought to keep generic versions of its film formulation of the drug off the market longer. Janet Woodcock, MD, director of the FDA's Center for Drug Evaluation and Research (CDER), wrote, "Reckitt's September 2012 announcement that it would discontinue marketing of the tablet product… given its close alignment with the period in which generic competition for the product was expected to begin, cannot be ignored." The FDA also referred the case to the Federal Trade Commission (FTC) because generic drug companies accused Reckitt of anti-competitive actions.
- The FDA approved two generic tablet versions of this drug, one by **Amneal Pharmaceuticals**, the other by **Actavis**.

Wound care – oxygen not helpful and may be harmful

A study published in ***Diabetes Care*** contradicts earlier studies that found exposure to pure oxygen could help wounds heal. Diabetics with severe foot ulcers got no benefit from oxygen chamber treatments and may even have experienced some harm. The foot ulcers did not heal faster, and the patients had three times the number of amputations as those getting standard care alone (7% vs. 2%).

The University of Pennsylvania Perelman School of Medicine researchers analyzed data on 6,259 diabetics, including 793 who got oxygen chamber therapy. At 16 weeks, 43% of oxygen patients vs. 50% of standard care patients had fully healed.

REGULATORY NEWS

EASD urges CE Mark process overhaul

The European Association for the Study of Diabetes (EASD) called for an urgent overhaul of the current CE Mark process for medical devices in Europe, saying that the current system could result in situations that may "seriously threaten the lives of people with diabetes because of its inadequacies." EASD noted: "There is a low level of regulation and control of medical devices in the European Union…[which poses] a continuous threat to the health of people with diabetes." It was especially critical of the lack of postmarketing surveillance and the less-than-rigorous approval process for devices compared to drugs, pointing to the "disastrous events" associated with hip implants and the PIP breast implants as examples of the "inefficiency of the current system."

In diabetes, EASD sharply criticized the level of quality control for insulin pumps and blood glucose monitoring systems, calling the quality control of both "ineffective." EASD said it would work closely with registries in Europe to develop models on how to continuously evaluate insulin pumps, saying, "Only those insulin pumps which undergo and pass such continuous evaluation and inspection should be approved for use and reimbursement by medical health insurance companies."

In the future, EASD wants the evaluation of glucose sensors and closed-loop systems to include intense collaboration with diabetes specialists. The EASD proposed:

- Medical devices in diabetes care be evaluated by independent research institutions, using the ISO-norm.
- Devices meet not only *in vitro* standards but also be evaluated in real-life settings.
- Continuous postmarketing surveillance of random samples.

FDA opioid abuse fix: Voluntary physician education

Writing in an FDA blog, FDA Commissioner Margaret Hamburg, MD, encouraged doctors to get more training in how to prescribe these painkillers, writing, "FDA is extremely concerned about the inappropriate use of opioids, which has reached epidemic proportions in the U.S., becoming a major public health challenge. While much of the problem is attributable to illicit use…our nation's front-line healthcare professionals, especially physicians and other prescribers, can play an important role in efforts to reduce this trend."

Dr. Hamburg called it "critically important to facilitate prescribers' education." She said several medical societies agreed to distribute the letter to their members, while the FDA will

distribute it to its contact list. In the letter, the FDA urges prescribers to take advantage of voluntary training on opioid prescribing, which became available on March 1, 2013, either low-cost or free through accredited continuing education activities supported by independent education grants (i.e., industry).

All of this is part of the risk evaluation and mitigation strategy (REMS) that the FDA imposed on July 2012, to address the misuse, abuse, and addiction related to extended-release (ER) and long-acting (LA) opioids.

FDA tidbits

- CDER is setting up a new drug quality office that will enforce *existing* quality standards instead of creating new quality requirements.
- The FDA proposed changes to the requirements for clinical trials of medical devices conducted outside the U.S. Among the changes: Manufacturers will be required to provide documentation of informed consent as well as on trial evaluation and approval by an independent ethics panel. The Agency is accepting comments through May 28.

FDA approvals/clearances

- **ARTHROCARE's SpeedLock HIP Knotless Fixation system**, an implantable device for use in soft tissue bone fixation in the hip, was cleared for use.
- **BAYER's Stivarga (regorafenib)** received expanded approval to treat patients with advanced gastrointestinal stromal tumors (GIST) that cannot be surgically removed and no longer respond to other FDA-approved treatments. Stivarga was already approved to treat metastatic colorectal cancer.
- **BIOTRONIK's Lumax 740 DX System**, a single-lead implantable cardioverter defibrillator (ICD), was cleared for use.
- **INSULET's OmniPod** – A new, smaller, and lighter version of this insulin pump for Type 1 diabetics was approved.
- **MEDTRONIC's Resolute Integrity stent** – New 34 mm and 38 mm lengths were approved for treating coronary artery disease in diabetics with this zotarolimus-eluting stent.
- **OTSUKA and LUNDBECK's Abilify Maintena (injectable aripiprazole)** – A new formulation of this antipsychotic was approved as a once-monthly injection to treat schizophrenia.
- **ROYAL PHILIPS ELECTRONICS' MicroDose SI technology**, a full-field digital mammography screening system, received 510(k) clearance.
- **SURGICAL THEATER's Selman Surgery Rehearsal Platform**, which provides a pre-surgery rehearsal for doctors in spine and cerebral surgery with 3D models showing the interaction between surgical tools and tissue, was cleared for use.
- **TANDEM DIABETES CARE's t:connect**, a diabetes management software, was cleared for use with the t:slim insulin pump.

FDA recalls/warnings

- **ABBEY COLOR**, an industrial-dye manufacturer, received a warning letter from the FDA for failing to ensure adequate purity of the water it uses when making fluorescein, a dye used in ophthalmic imaging.
- **AD-TECH MEDICAL INSTRUMENTS' Macro Micro Subdural Electrodes** were recalled over a concern they were not flush with the silastic surface.
- **LUMENIS' VersaCut tissue morcellator** – A Class I recall was initiated due to a labeling error that could cause the tubing to be hooked up backwards, potentially causing air embolisms and even death. The company is relabeling the product and issuing a new Operator's Manual.
- **MEDTRONIC's CoreValve** – One of the principal investigators in the U.S. pivotal trial of this transcatheter aortic valve replacement (TAVR) received a warning letter from the FDA that cited serious violations in the treatment of patients in the trial, including failure to obtain informed consent and two deaths that were not properly reported to the FDA, and failure to maintain complete and accurate records.

European regulatory news

- **ALEXZA PHARMACEUTICALS' Adasuve (inhaled loxapine)** was approved by the European Commission to treat mild-to-moderate agitation in adult patients with schizophrenia or bipolar disorder.
- **NOVARTIS' Ilaris (canakinumab)** has been approved by the European Commission for use by patients with acute gouty arthritis. The drug works by blocking the protein interleukin-1 beta, which is believed to be the source of inflammation. Ilaris is already used to treat those suffering from another inflammatory disorder, cryopyrin-associated periodic syndromes. Citing concerns about side effects, U.S.

officials rejected the drug in 2011 as a treatment for gouty arthritis.

- **NXSTAGE MEDICAL** has earned CE Mark approval to market its enhanced System One portable hemodialysis device, which now features high-flow capabilities, in Europe. The approval comes shortly after the company received the EU nod for use of the same device in nocturnal hemodialysis.

- **ROCHE's 454 GS Junior –** The Red Cross Blood Transfusion Service in Upper Austria obtained accreditation to use this next-generation sequencer in tissue-typing for stem cell transplants.

- **SANOFI's Hexyon/Hexacima (DTaP-IPV-Hib-HepB vaccine) –** The European Medicines Agency's Committee for Medicinal Products for Human Use recommended approval of this six-in-one pediatric vaccine.

- **U.K. patent law –** Regulators are considering a change to patent laws in the life sciences sector that would remove limits on studies of new, patented medications and allow tests of new medicines involving patented treatments. "The great frustration has been that we have an excellent research base but we need to ensure that our innovations and bright ideas can get to market," said Science Minister David Willetts. The change could come by October.

Regulatory news from other countries

- ***Argentina:*** The government enacted changes to its medical device regulations that are expected to make the approval process for Class II, III, and IV devices clearer.

- ***China:*** The State Food and Drug Administration announced plans for wide-ranging changes in its drug regulatory process, including an update of the generic drug program, improvements in clinical trials, and encouragement of more pediatric drugs.

2013 FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
March 1	**Zogenix's Zohydro** (extended-release hydrocodone) for chronic pain	PDUFA date ***Delayed for "several weeks"***
March 4	**Depomed's gabapentin** and **Noven Therapeutics' paroxetine** – both to treat moderate-to-severe vasomotor symptoms of menopause	FDA's Reproductive Health Drugs Advisory Committee
March 5	Efficacy vs. cancer risk with calcitonin-salmon products **– Novartis' Miacalcin** (calcitonin-salmon – injection and nasal spray) and **Upsher-Smith Laboratories' Fortical** (calcitonin-salmon recombinant nasal spray) – for the treatment of postmenopausal osteoporosis	Joint meeting of the FDA's Reproductive Health Drugs Advisory Committee and the FDA's Drug Safety and Risk Management Advisory Committee
March 7	**GlaxoSmithKline's Breo Ellipta** (fluticasone furoate + vilanterol), a dry powder inhaler for chronic obstructive pulmonary disease (COPD)	FDA's Pulmonary-Allergy Drugs Advisory Committee
March 14	Discussion of the FDA's **draft risk assessment model** for potential exposure to the variant **Creutzfeldt-Jakob disease (vCJD) agent in red blood cells for transfusion** in the U.S.	FDA's Transmissible Spongiform Encephalopathies Advisory Committee
March 17	**Bristol-Myers Squibb** and **Pfizer's Eliquis** (apixaban,) an oral anticoagulant to prevent stroke in atrial fibrillation patients	PDUFA date
March 18	**Pharmaxis' Bronchitol** (mannitol) for cystic fibrosis	PDUFA date
March 20	**Abbott's MitraClip** for mitral valve repair	FDA's Circulatory System Devices Advisory Committee
March 22	**Cangene's BAT** (botulinum antitoxin), an anti-bioterrorism agent	PDUFA date
March 28	**Biogen Idec's BG-12** (dimethyl fumarate) for multiple sclerosis	PDUFA date (extended from December 28, 2012)
March 31	**Johnson & Johnson's Invokana** (canagliflozin), a SGLT2 inhibitor to treat Type 2 diabetes	PDUFA date
April 8	**Bausch & Lomb's Trulign Toric** implantable intraocular lens for post-cataract surgery patients	FDA's Ophthalmic Devices Advisory Committee
April 11	Potential effects of extreme weather and natural disasters on **medical device safety and quality**	FDA's Device Good Manufacturing Practice Advisory Committee
April 15	**MAP Pharmaceuticals' Levadex** (dihydroergotamine), inhaled migraine drug	PDUFA date
April 25	Reclassification of **methotrexate enzyme immunoassays, phencyclidine (PCP) enzyme immunoassays, and PCP radioimmunoassays**	FDA's Clinical Chemistry and Clinical Toxicology Devices Advisory Committee
April 26	Reclassification of **isoniazid test strips**	FDA's Clinical Chemistry and Clinical Toxicology Devices 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	**Raptor Pharmaceutical's Procysbi** (cysteamine bitartrate delayed-release, RP-103) to treat nephropathic cystinosis	PDUFA date (extended from January 30, 2013)
May 2	**Aveo and Astellas' Tivopath** (tivozanib) for advanced renal cell carcinoma	FDA's Oncologic Drugs Advisory Committee
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 tba	**PET imaging** of brain beta-amyloid	CMS coverage decision expected
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
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
December 18	**GlaxoSmithKline** and **Theravance's Anoro** (umeclidinium bromide + vilanterol) for COPD	PDUFA date