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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SHORT TAKES

- **AETERNA ZENTARIS' perifosine –** The company discontinued a Phase III trial of this investigational multiple myeloma drug for futility. The independent data safety monitoring committee said early data from the trial indicated that adding perifosine, which has orphan drug and fast track status, to **Roche's Velcade** (bortezomib) + dexamethasone was unlikely to increase progression-free survival (PFS) – the primary endpoint – in relapsed/refractory multiple myeloma.

- **Amyotrophic lateral sclerosis (ALS) –** A 161-patient study published in ***The Lancet*** found that 18 months of lithium did not prolong survival in ALS patients better than placebo (50% 18-month survival with placebo vs. 59% with lithium).

- **Antipsychotics –** A meta-analysis of 14 studies, published in ***PLOS Medicine***, found that adding an antipsychotic in patients with depression who were not fully responding to antidepressants provided little additional benefit but added new side effects.

- **ASTRAZENECA's selumetinib (AZD-6244) –** This MEK1/2 inhibitor missed the primary endpoint in a Phase II trial in recurrent endometrial cancer, failing to meet the protocol-defined criteria despite showing a clinical benefit rate of 32%, a response rate of 6%, and a 6-month progression-free survival rate of 22%.

- **ATHENAHEALTH** acquired **Epocrates**, a mobile application developer.

- **BIOGEN IDEC's** recombinant factor VIII Fc fusion protein (rFVIIIFc) – The company submitted a biologics license application (BLA) to the FDA for rFVIIIFc to treat hemophilia A.

- **CHIMERIX's CMX-001** received fast track status from the FDA for prevention of cytomegalovirus infection. It already had fast track status for smallpox and adenoviral disease in post hematopoietic stem cell transplant patients.

- **Cleveland Clinic** is working with **Community Health Systems** (CHS) in an effort to improve care quality and lower costs at CHS' 130+ community hospitals in 29 states.

- **DR. REDDY'S LABORATORIES' halometasone 0.05% + fusidic acid 2% –** A randomized, open-label Phase III study published in the ***Indian Journal of Dermatology*** found that a cream with these two agents has similar efficacy in improving symptoms of eczema and pruritus to a cream with betamethasone 0.12% + neomycin sulfate 0.5%, but the halometasone/fusidic acid cream was more effective in treating infected lesions.

- **INVIVO THERAPEUTICS** ***resubmitted*** an investigational device exemption (IDE) application to start trials of its bio-scaffold for treating spinal cord injuries. The company also is hoping to get a humanitarian use device classification.

- **Mesenchymal stem cells** – A study by Irish researchers, published in ***Diabetes***, found that mesenchymal stem cells, when used with a biomaterial made from collagen, could boost wound healing and help prevent amputations in patients with diabetic foot wounds.

- **NEOS THERAPEUTICS' NT-0202** – The company filed a 505(b)(2) application for this investigational, once-daily, extended-release, orally disintegrating tablet version of amphetamine polistirex to treat attention-deficit/hyper-activity disorder (ADHD).

- **ORION PHARMA's ORM-12741** – A 100-patient study to be presented at the American Academy of Neurology meeting found that this investigational drug modestly improved episodic and overall memory in patients with moderate Alzheimer's disease when added to **Forest Laboratories' Namenda** (memantine) for three months.

- **PRESIDIO PHARMACEUTICALS** and **BOEHRINGER INGELHEIM** signed a non-exclusive agreement to collaborate on a 12-week Phase IIa trial, beginning in 2Q13, in patients with hepatitis C genotype 1a (HCV-1a) of all-oral, interferon-free, triplet direct-acting antiviral therapy with Presidio's PPI-668 (a NS5A pan-genotypic polymerase inhibitor) + Boehringer's faldaprevir (BI-201335, a protease inhibitor) + Boehringer's BI-207127 (a NS5B polymerase inhibitor) with or without ribavirin. Presidio will run the trial in "close collaboration" with Boehringer. SVR4 and SVR12 results are expected in 4Q13.

- **ROCHE/GENENTECH's Herceptin (trastuzumab)** – A meta-analysis of 9,020 breast cancer patients, published in the ***Annals of Oncology***, found that women who take Herceptin for HER2+ breast cancer have a significantly increased risk for development of metastases in the central nervous system (CNS) as the site of first recurrence (2.56% vs. 1.94% with no Herceptin).

- **SANOFI's Plavix (clopidogrel)** – The U.S. Department of Justice is investigating the company's disclosures to the FDA about variable responses to this anticoagulant that indicated some patients had reduced efficacy prior to the FDA boxed warning in 2010 that metabolism is reduced in patients with the CYP2C19 genotype.

- **SHIRE** bought **Premacure**, a Swedish company with an investigational insulin-like growth factor 1 (IGF-1) treatment for prevention of retinopathy of prematurity.

- **SINOVAC BIOTECH's Enterovirus 71 (EV71) vaccine** – In preliminary data from a very large Phase III of this vaccine to prevent hand, foot, and mouth disease (HFMD) in infants age 6-35 months, this vaccine was 95.4% effective. The side effect rate in infants (2.2%) was similar to placebo and not statistically significant. Sinovac plans to submit the vaccine to Chinese regulators soon.

- **Swine flu vaccine (H1N1)** – Getting the swine flu vaccine increases the risk of Guillain-Barré syndrome, but very, very little – an additional 1.6 extra cases for every 1 million people vaccinated. That was the finding of a study by the U.S. National Vaccine Program Office, which was published in ***The Lancet***. The researchers concluded that the findings should reassure the public that the vaccine's benefits outweigh the risks.

NEWS IN BRIEF

BOEHRINGER INGELHEIM's Pradaxa (dabigatran) – FDA says bleeding not a big problem

In an article in the ***New England Journal of Medicine***, FDA officials tried to allay concerns about excessive bleeding with this direct thrombin inhibitor vs. warfarin, saying that the high number of reports about Pradaxa-induced bleeding are most likely due to increased sensitivity and vigilance, not an inherent problem with the drug. They wrote, "We believe that the large number of reported cases of bleeding associated with dabigatran provides a salient example of stimulated reporting."

The FDA officials said postmarketing reports of bleeding received through the FDA Adverse Event Reporting System raised questions about the safety of Pradaxa because the rates were higher than seen in the pivotal RE-LY trial. The Agency investigated the possibility that Pradaxa may have been used differently or in different patient populations than those in RE-LY, but a review found "no indication that dabigatran was not being used in accordance with its labeled directions."

GLP-1 agonists and DPP4 inhibitors – FDA investigating risk of pancreatitis

The FDA announced it is evaluating new, unpublished findings by academic researchers that suggest an increased risk of pancreatitis and pancreatic duct metaplasia in Type 2 diabetics treated with these incretin mimetics. These findings were based on examination of a small number of pancreatic tissue specimens taken from patients after they died from unspecified causes. The FDA asked the researchers to provide their methodology as well as the tissue samples so the Agency can conduct its own investigation.

All of the drugs in this class are under scrutiny:

- **alogliptin** (**Takeda's Nesina, Kazano,** and **Oseni**)
- **exenatide** (**Bristol-Myers Squibb/Amylin's Byetta** and **Bydureon**)
- **linagliptin** (**Boehringer Ingelheim's Tradjenta** and **Jentadueto**)
- **liraglutide** (**Novo Nordisk's Victoza**)
- **saxagliptin** (**Bristol-Myers Squibb and Astra-Zeneca's Onglyza, Kombiglyze XR**)
- **sitagliptin** (**Merck's Januvia, Janumet, Janumet XR,** and **Juvisync**)

The FDA will participate in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and National Cancer Institute's (NCI) Workshop on Pancreatitis-Diabetes-Pancreatic Cancer in June 2013 "to gather and share additional information." Meanwhile, the labels for these drugs already contain warnings about the risk of acute pancreatitis, though the labels do not talk about the potential risk of pre-cancerous findings since the FDA has not determined whether it believes these drugs may cause or contribute to the development of pancreatic cancer.

In February, an analysis of data from seven BlueCross/BlueShield plans, published in ***JAMA Internal Medicine***, found these drugs double the risk of acute pancreatitis, which in turn was linked to cancer and kidney failure.

Questions about pancreatitis and incretin mimetics are not new. A year after Byetta was first approved in 2005, the issue was raised. At the European Association for the Study of Diabetes (EASD) meeting in 2006, ***Trends-in-Medicine*** reported that officials from Amylin and Lilly (then a partner) insisted there was no signal of a problem with pancreatitis and that the pancreatitis rate with Byetta was the same as the background rate in the general diabetic population, but some doctors were worried about it.

Exenatide (exendin-4) was discovered in Gila monster venom, and according to several articles on the history of Byetta, the victims of Gila monster bites can develop pancreatitis due to over-stimulation of the pancreas.

In April 2009, after the advisory committee meetings on Victoza and Onglyza, ***Trends-in-Medicine*** reported that Mary Parks, MD, director of the FDA's Division of Metabolism and Endocrinology Products (DMEP), Center for Drug Evaluation and Research (CDER), was asked about the FDA's current level of concern about pancreatitis with Byetta or Victoza, and she said, "That is being evaluated…in this and all GLP-1s and all the incretin-based therapies. I don't think at this point we have enough clinical experience with liraglutide to be able to compare [it to Byetta]…It hasn't been compared in an adequate trial to exenatide…What [comparative] studies have been done are short duration…Setting aside comparative studies, we don't have enough clinical exposure with liraglutide to comment on the risk of pancreatitis…The pancreatitis with Byetta is from postmarketing…I think it is safe to assume some expectation of additional data on pancreatitis [will be requested]…I'd hedge to say a requirement."

Hip implants
– blood cobalt levels signal time for replacement

Measuring cobalt ion levels in blood may help identify which patients will need to have their metal-on-metal hip implant replaced. A retrospective study by U.K. researchers, published in ***BMJ Open***, found significantly higher cobalt ion levels in asymptomatic patients who later needed revision of **Johnson & Johnson/DePuy** and **Smith and Nephew** metal-on-metal hip implants.

The researchers calculated that the seven-year risk when the blood cobalt level was ≥10 µg/L was:

- 21.8% for men and 42.7% for women with J&J's **ASR** hip.
- 2.6% for men and 5.8% for women with Smith & Nephew's **Birmingham** hip.

This is the first evidence that doctors may be able to screen patients with a blood test to determine who will need re-surgery. Neither the FDA nor U.K. health authorities currently recommend routine metal ion testing in patients with a metal-on-metal hip implant.

INTUITIVE SURGICAL's da Vinci
– ACOG warns *against* use except in rare cases

The American Congress of Obstetricians and Gynecologists (ACOG) advised that a robotic hysterectomy "shouldn't be the first or even the second choice" for most women. In a statement posted on the ACOG website, President James Breeden, MD, said, "Robotic surgery is not the only or the best minimally-invasive approach for hysterectomy. Nor is it the most cost-efficient. It is important to separate the marketing hype from the reality when considering the best surgical approach for hysterectomies…There is no good data proving that robotic hysterectomy is even as good as – let alone better than – existing, and far less costly, minimally-invasive alternatives."

Currently ~10% of hysterectomies are being done with the robot, which adds ~$2,000 to each procedure. Dr. Breeden estimated that doing all hysterectomies with the robot would add up to $2 billion to healthcare costs annually. He said da Vinci should be reserved for "unusual and complex clinical conditions" where improved outcomes have been demonstrated.

Parkinson's disease – three promising studies

Three studies to be presented at the American Academy of Neurology meeting look promising in Parkinson's:

- **Chelsea Therapeutics' Northera (droxidopa).** A 225-patient, 10-week study that found that over eight weeks, Parkinson's disease patients given this hypotension drug had a clinically meaningful, two-fold decrease in their dizziness and lightheadedness vs. placebo. The droxidopa patients also had fewer falls per week (0.38 vs. 1.73).
- **Biotie Therapies** and **UCB's tozadenant (SYN-115).** A 420-patient, 12-week study found that giving this adenosine 2a (A2a) receptor inhibitor to Parkinson's disease patients on levodopa whose "off time" per day had increased to an average of six hours reduced that off time by about an hour per day (at the highest two of the four doses tested). Tozadenant did not increase dyskinesia (involuntary movements).
- **Teva's Azilect (rasagiline, AGN-1135).** A 321-patient, 18-week study found that patients with early Parkinson's disease whose symptoms were not well-controlled by a dopamine agonist were helped with this irreversible inhibitor of monoamine oxidase (MAO). At Week 18, the rasagiline patients had improved by 2.4 points on a Parkinson's disease rating scale vs. placebo. Rasagiline was well tolerated, with adverse events similar to placebo.

REGULATORY NEWS

Medicare to cover some FDG-PET scans

CMS issued a proposed decision memo that said Medicare will cover FDG-PET scans done to monitor a malignant tumor in routine practice, but not in prostate cancer. CMS' proposed reimbursement is for a single FDG-PET scan, with the final coverage determination to be made by local Medicare contractors.

A scan, which measures the rate of glucose metabolism non-invasively in tissues, can help doctors plan a patient's treatment. Because malignant cells metabolize glucose faster than normal cells, the tumors become easily identifiable by FDG-PET imaging.

In prostate cancer, CMS did not believe there was sufficient evidence that FDG-PET is reasonable and necessary. In fact, for prostate cancer CMS said, "We are concerned that the FDG-PET results may be misinforming patient care."

CMS is accepting comments on the proposed policy.

FDA to ease rules for Alzheimer's drug approvals

In an article published in the ***New England Journal of Medicine***, FDA officials outlined plans to make it easier to get new Alzheimer's disease drugs approved. Under the new rules, drugs aimed at Alzheimer's patients with early-stage disease might be eligible for accelerated approval based on improvements in their performance on memory or reasoning tests alone. The drugs would no longer need to show pre-approval that they improve daily functioning as well. However, post-approval studies would be required to show functional benefit. Under current rules, Alzheimer's drugs must show an improvement on both memory and function before approval.

The new guidance also:

- Will allow the use of biomarkers to select patients for trials in early-stage Alzheimer's disease, such as beta-amyloid on PET or beta-amyloid and tau proteins in cerebrospinal fluid (CSF), in conjunction with clinical criteria.
- Suggests use in overt dementia patients of a single scale that combines assessment of both cognition and function, such as the score on the Clinical Dementia Rating Sum of Boxes (CDR-SB).
- Would ***not*** allow approval based on a change in a single biomarker.

FDA under pressure on generic opioids

The National Association of Attorneys General wrote the FDA asking the Agency to require that generic opioid painkillers be made tamper-resistant. And some members of Congress have been pressing the FDA on the same issue. However, don't count on the pressure to prevail. Remember that (1) no opioid has yet been proven to the FDA's satisfaction to be sufficiently less abusable to earn that label, and (2) the Canadian health minister allowed generic oxycodone (**Purdue's OxyContin**) despite a plea from all the provincial governments not to do so.

House hearings on FDA regulation of mobile apps

House Energy and Commerce subcommittees will hold hearings on March 19-21, 2013, to review how mobile health

applications should be regulated by the FDA. Earlier this month, seven members of the committee sent a letter to FDA Commissioner Margaret Hamburg, MD, expressing concerns about if and how the FDA intends to oversee medical apps for computers, iPhones, iPads, and other devices, noting that app developers could be subject to a tax under the Affordable Care Act if the FDA classifies their apps as medical devices.

On March 19 the subcommittee on communications and technology will hear from developers about how consumers are using existing health and fitness apps. On March 20 the subcommittee on health will hear from healthcare practitioners and patients about how they use these kinds of apps for diagnoses. On March 21 the subcommittee on oversight and investigations will hear from FDA and HHS officials.

Office of Generic Drugs chief abruptly resigns

Trouble in CDER city? Greg Geba, MD, MPH, director of the FDA's Office of Generic Drugs (OGD), resigned, effective March 15, 2013, after just eight months in the position. In his departure email, the reasons he cited for leaving other than the usual family issues were: the shift in OGD's resources from extending "generics across the entire therapeutic spectrum" to other "extremely important efforts of the chemistry group in moving to OPQ [the Office of Pharmaceutical Quality], which I entirely support" – that is, the consolidation of generic drug review with that of new drugs into the new combined office.

Dr. Geba noted that in September 2012 the backlog of generic applications was 2,762 but last week was down to 2,166, but he also pointed out that the organization "remains significantly understaffed," though >100 associates are being hired in the next few months.

CDER director Janet Woodcock, MD, also emphasized that Dr. Geba supports the "quality evolution in CDER [but] nonetheless saw this movement as creating challenges for implementing his original and full vision for OGD's remit." Dr. Woodcock said she will serve as the acting OGD director until a replacement is found.

FDA approvals/clearances

- **ALPHATEC SPINE's Alphatec Solus**, an internal fixation system for spinal fusion, received 510(k) clearance.
- **INVENDO MEDICAL's C20 single-use colonoscopy device and its SC20 colonoscope**, a handheld tool designed to be used with computer-aided technology to minimize stress on the colon wall, both received 510(k) clearance.
- **NAVIDEA BIOPHARMACEUTICALS' Lymphoseek (technetium Tc 99m tilmanocept)**, a radioactive diagnostic imaging agent to help doctors locate lymph nodes in patients with breast cancer or melanoma who are undergoing surgery to remove tumor-draining lymph nodes, was approved.
- **OPTOS' OCT SLO system** – The company received 510(k) clearance to incorporate microperimetry testing into this optical coherence tomography (OCT) device.
- **QUIDEL's Molecular RSV + hMPV test**, which identifies human metapneumovirus and respiratory syncytial virus – and differentiates them from each other – received 510(k) clearance.
- **RTI BIOLOGICS** received 510(k) clearance for its porcine dermis implantable scaffolding device for use in hernia repair and other soft tissue fixation procedures.

FDA recalls/warnings

- **BOSTON SCIENTIFIC/CAMERON HEALTH's S-ICD** – The company sent a Dear Doctor letter warning physicians about potential fuse malfunctions with these lead-free implantable defibrillators. The company is offering a software update to resolve the issue and is advising that patients with a recently implanted S-ICD visit their doctor for an update.
- **FRESENIUS MEDICAL CARE NORTH AMERICA** received a warning letter saying it failed to adequately perform design validation trials of sterilized dialyzers at its facility in Ogden UT.
- **Latex** – Manufacturers were warned to stop labeling products as "latex-free," saying the claims were "scientifically inaccurate." Instead, the FDA suggested labeling the products as "not made with natural rubber latex."
- **PFIZER's Zithromax (azithromycin)** – The FDA issued a drug safety alert to doctors, warning them that this antibiotic can cause abnormal changes in the electrical activity of the heart, potentially leading to a fatal irregular heart rhythm (torsades de pointes). Patients with known risk factors – e.g., QT prolongation, low potassium or magnesium levels, bradycardia, etc. – are particularly at risk. In May 2012, the FDA advised that a study had found an increase in cardiovascular deaths with azithromycin vs. amoxicillin, ciprofloxacin, and placebo.
- **STRYKER** received a warning letter for quality-control issues at its Michigan plant for not notifying the FDA about a product recall and for marketing medical devices (e.g., the Neptune Waste Management system) without 510(k) clearance.

European regulatory news

- **ACTIVARTIS' AV-0113**, a cancer immunotherapy, was granted orphan drug status for treating glioma.
- **Drug review fees** – The European Medicines Agency (EMA) plans to increase the fees charged for drug reviews starting in April 2013 by ~2.6%, and it will reduce the current 75% discount given for orphan drugs.
- **JOHNSON & JOHNSON's Motilium (domperidone)** – At the request of Belgian regulators, the EMA is reviewing this antiemetic drug due to concerns about possible cardiac adverse events, including QT prolongation and arrhythmias. The Belgian authorities suggested the drug be contra-indicated in patients with QT prolongation, congestive heart failure, and other underlying cardiac diseases. Motilium was rejected by the FDA twice (in 1985 and 1991).
- **MERIT MEDICAL SYSTEMS' Embosphere Micro-spheres**, which relieve the symptoms of benign prostatic hyperplasia (BPH) by obstructing blood flow in selected vessels around the prostate, received a CE Mark.
- **NANOSPHERE's Gram-Negative Blood Culture (BC-GN) test** for rapid diagnosis of bacteria that can trigger bloodstream infections received a CE Mark.
- **TAKEDA's vedolizumab** was submitted to the EMA to treat moderately-to-severely active ulcerative colitis and Crohn's disease.
- **U.K.'s Medicines and Healthcare products Regulatory Agency (MRHA)** launched an Innovation Office aimed at helping companies with innovative products navigate the regulatory pathways for devices, drugs, and other medical products. Applications will be able to be filed online.
- **Warning labels** – Starting in January 2014, the European Commission will require certain high-risk drugs and biologics to carry a mandatory inverted black triangle on their information leaflets. Existing inventory will not need to be relabeled, but new production will have to carry the warning sign.

Regulatory news from other countries

Ghana: The Food and Drugs Authority of Ghana alleged that three Ghanaian pharmaceutical companies – including **Lymens Medical Supplies**, **Sarkuff Pharmacy**, and **Osons Chemist** – imported fake, substandard, and contaminated medicines. The drugs affected include substandard and contaminated OxyContin injections, ergometrine injections with no active pharmaceutical ingredients, and fake oxytocin, ergometrine, and quinine injections.

2013 FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
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 19-21	FDA regulation of **mobile health applications** for smartphones and tablets	House Energy and Commerce subcommittee hearings
March 20	**Abbott's MitraClip** for mitral valve repair	FDA's Circulatory System Devices Advisory Committee
March 21	**Titan Pharmaceuticals' Probuphine** (buprenorphine subdermal implant) to treat opioid dependence	FDA's Psychopharmacologic Drugs 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 Sefelsa** (gabapentin extended-release), a hot-flash treatment (formerly known as Serada)	PDUFA date
June 20	**Dainippon Sumitomo Pharma/Sunovion Pharmaceuticals' Latuda** (lurasidone), a schizophrenia drug for use in treating bipolar disorder	PDUFA date
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 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
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