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 FDA's General and Plastic Surgery Devices Advisory Committee meeting on **Allergan's Juvéderm Voluma XC** dermal filler and the FDA's Oncologic Drugs Advisory Committee meeting on **Aveo Pharmaceuticals** and **Astellas' Tivopath** (tivozanib) for advanced renal cell carcinoma.

SHORT TAKES

- **ABBOTT's MitraClip –** The company asked the Centers for Medicare & Medicaid Services (CMS) for a new technology add-on payment for this mitral valve repair device, and CMS is seeking public comments on whether MitraClip meets the newness, the cost, and the substantial clinical improvement criteria. *This is probably a moot issue for now since it is likely to be a long time before the FDA approves MitraClip.*

- **AVEO PHARMACEUTICALS and Astellas' Tivopath (tivozanib) –** The FDA's Oncologic Drugs Advisory Committee (ODAC) voted 13-1 that another trial is needed before this tyrosine kinase inhibitor could be approved to treat renal cell carcinoma.

- **BAYER** is buying **Conceptus**, giving it **Essure**, a non-surgical, permanent birth control product to add to its women's health portfolio.

- **IMPAX LABORATORIES' Rytary (IPX-066, carbidopa and levodopa extended-release) –** Impax ended its collaboration with **GlaxoSmithKline** on this investigational Parkinson's disease drug, citing delays in regulatory approvals and repeated launch-date postponements in the countries where GSK holds the marketing rights.

- **MYLAN**'s new senior vice president of strategic global quality and regulatory policy will be Deborah Autor, the FDA's former deputy commissioner for global regulatory operations and policy, effective June 1, 2013.

- **PFIZER's ertugliflozin (PF-04971729) –** Pfizer and **Merck** agreed to collaborate on development and marketing of this investigational SGLT2 inhibitor for Type 2 diabetes. The drug will begin Phase III trials later this year and will also be studied in combination with **Merck's Januvia** (sitagliptin) and **Janumet** (sitagliptin + metformin).

- **QIAGEN** is buying **Ingenuity Systems**, which provides software analysis and interpretation of complex biological data.

- **SANOFI PASTEUR and KALOBIOS PHARMACEUTICALS' KB-001A**, an experimental treatment for *Pseudomonas aeruginosa*-related pneumonia in ventilator patients, received fast track status from the FDA.

- **SORIN's Perceval S –** The FDA told Sorin it can begin a trial of this sutureless aortic tissue valve.

- **TIGENIX's Cx-611 –** The company released positive results from a single-blind, dose-escalation, placebo-controlled, Phase IIa trial of this allogeneic, mesenchymal, adipose-derived stem cell therapy in 53 patients with refractory rheumatoid arthritis (RA). The treatment appeared safe, and there was at least a hint of efficacy. Patients all got a disease-modifying anti-rheumatic drug (DMARD) ± Cx-611.

- **TITAN PHARMACEUTICALS and BRAEBURN PHARMACEUTICALS' Probuphine (buprenorphine implant) –** The FDA rejected this implant for opioid dependence, issuing a complete response letter asking for more data on higher doses and on training for doctors on insertion and removal of the implant.

NEWS IN BRIEF

ALLERGAN

- **Juvéderm Voluma XC.** The FDA's General and Plastic Surgery Devices Advisory Committee voted unanimously (7-0) that this dermal filler is safe, that it is effective, and that the benefits outweigh the risks.

- **DARPin.** The company said it plans to conduct another Phase II trial before moving to Phase III with this investigational macular degeneration drug, which will add another 1-2 years to the development timeline. This suggests that the drug may not last as long (3-4 months) as previously thought. There should be some Phase II data during Retina Day at the American Academy of Ophthalmology meeting in November 2013.

- **Bimatoprost.** The company also plans to conduct another Phase II trial of this drug in the hair growth indication – at an ~10x higher dose and a new formulation – before moving to Phase III, which delays this as well. There are also plans to study it in females.

Alzheimer's disease – research funding problems

In an article in ***Alzheimer Research Forum***, executive editor Gabrielle Strobel painted a troubling picture of funding for Alzheimer's research (**www.alzforum.org**). She said that one of the three key trials in pre-symptomatic Alzheimer's disease – Dominantly Inherited Alzheimer Network (DIAN) – is up and running and starting to treat patients with young-onset genetic Alzheimer's but is short of money, "Public funding is becoming so scarce that the DIAN researchers are increasingly asking industry to help move the project forward. DIAN's Pharma Consortium includes 10 pharmaceutical companies that have contracted to jointly support the development of clinical trials for people with autosomal-dominant AD, regardless of whether their own drug is currently being studied in a given DIAN trial."

She quoted Randall Bateman, MD, a neurologist from Washington University, as saying, "I am concerned that we may miss opportunities at several levels – scientific, power, collaborative – because of funding."

She also reported that investigators are making or considering several other changes to the DIAN trial, including:

- Shortening the trial by using an adaptive design. Currently, the trial is for two years followed by another four years of the most promising drug in the study. A new Phase II/III design has been adopted that eliminates the break between the current biomarker trial and the cognitive registration trial, speeding enrollment for Phase III.

- Comparing and reporting amyloid values with and without volume correction. Gray matter atrophy can make it appear there is less amyloid in a brain when it is really brain shrinkage.

- Cerebrospinal fluid tests on each individual would need to be performed at baseline and on subsequent samples using the same plate and in the same test run, not years apart on separate plates. DIAN plans to run all baseline and one-year samples together at the time of the interim analysis. It will re-run those samples together with end-of-study samples when the trial concludes.

The original DIAN grant was awarded in 2008 by the National Institute on Aging and covered 240 people. The trial is enrolling better than expected, with 330 people now enrolled and another 70 expected to enroll by the end of 2014. DIAN is applying for a five-year renewal, but the renewal is capped at the original 2008 funding levels, so there is a 160-patient shortfall in funding.

Breast cancer genetic testing – might not be as helpful as thought

A study presented at the IMPAKT Breast Cancer Conference in Belgium found that the most effective predictor of breast cancer recurrence >5 years after diagnosis for women with early-stage breast cancer is the clinical characteristics of the tumor (size, grade, lymph node involvement), ***not*** genetic testing.

The study compared the clinical treatment score, immunohistochemical marker testing, and three gene expression scores for ~10,000 postmenopausal women in the ATAC trial. All of the methods performed similarly during the first 5 years of the

study, but in the next 5 years, the clinical treatment score was the most accurate, though two genetic tests – PAM50 Risk of Recurrence (ROR) and the Breast Cancer Index (BCI) scores – added significantly to the clinical treatment score's prediction accuracy.

GILEAD SCIENCES

- **All-oral regimen works in just 8 weeks in HCV-1.** Shortly after the European Association for the Study of the Liver (EASL) meeting in Amsterdam, Gilead reported positive results from the Phase II LONESTAR trial of a once-daily, fixed-dose combination of sofosbuvir (GS-7977, an NS5B inhibitor) + ledipasvir (GS-5885, an NS5A inhibitor) in hepatitis C virus (HCV) patients with genotype 1. The trial had several arms, but they were all positive:
  - 8 weeks of sofosbuvir/ledipasvir (without ribavirin) = 95% (19 of 20) treatment-naïve patients achieved SVR8.
  - 8 weeks of sofosbuvir/ledipasvir + ribavirin = 100% (21 of 21) treatment-naïve patients achieved SVR8.
  - 12 weeks of sofosbuvir/ledipasvir + ribavirin = 100% (19 of 19) treatment-naïve patients achieved SVR4.
  - 12 weeks of sofosbuvir/ledipasvir + ribavirin = 95% (20 of 21) of prior treatment failures achieved SVR4. One patient was lost to follow-up.
  - 12 weeks of sofosbuvir/ledipasvir (without ribavirin) = 95% (18 of 19) of prior treatment failures achieved SVR4. One patient relapsed.

Gilead also plans to start a third Phase III trial of sofosbuvir + ledipasvir, ION-3 – an open-label study with and without ribavirin in 600 treatment-naïve, non-cirrhotic HCV-1 patients. There will be three arms: 8 weeks of sofosbuvir/ledipasvir + ribavirin, 8 weeks of sofosbuvir/ledipasvir without ribavirin, and 12 weeks of sofosbuvir/ledipasvir without ribavirin. The primary endpoint will be SVR12, and the study will assess non-inferiority of the 8-week regimens to the 12-week regimen. The ongoing ION-1 and ION-2 trials are testing 12- and 24-week regimens of sofosbuvir/ledipasvir ± ribavirin.

- **Cobicistat and elvitegravir.** Even though these two drugs are approved as part of Gilead's quad pill **Stribild**, the FDA rejected both of them as individual HIV drugs, citing quality control problems at the company's plant and pointing to problems with documentation and quality testing during recent inspections.

Hepatic encephalopathy – shunt reduction can help

A retrospective review of 37 European patients, presented at the EASL meeting, found that a shunt can ease hepatic encephalopathy in cirrhotic patients. Another study at EASL found that hepatic encephalopathy patients who received a transjugular intrahepatic portosystemic shunt (TIPS) for preventing variceal bleeding benefited from a shunt reduction procedure. A number of centers in Europe reportedly have started doing shunt reduction procedures in selected patients, and a review of those patients found many (at least in the short term) had their hepatic encephalopathy eliminated, with hospitalizations reduced.

Omega-3 fatty acids – might help preserve memory in healthy people

The REGARDS study, supported by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health and by the Department of Health and Human Services – published in ***Neurology*** – found that eating omega-3 fatty acids and avoiding meat and dairy may help preserve memory – but not in diabetics.

Researchers collected dietary information from 17,478 African Americans and Caucasians (average age 64) to see how closely they adhered to a Mediterranean diet. They were also given tests that measured memory and thinking abilities over an average of four years. Healthy people who closely followed the Mediterranean diet were 19% less likely to develop thinking/memory problems.

There was no significant difference in declines between African Americans and Caucasians, but the Mediterranean diet did not protect diabetics.

PFIZER's Xalkori (crizotinib) – test for ALK early, conserve tissue

On a webcast on molecular testing for lung cancer, sponsored by Pfizer and the Association of Community Cancer Centers, experts discussed new recommendations about testing lung cancer patients for EGFR and ALK. The messages they were trying to get out to the community included:

- Do genetic testing early; don't wait.
- Do EGFR and then ALK testing before other tests to preserve limited tissue.
- Pathologists and oncologists need to work together.

One speaker said, "Historically, we used to make some judgment on who we would genotype based on clinical characteristics, smoking status, or ethnicity, but that has largely gone away. Today, in our clinic we genotype all non-squamous cell lung cancer patients, and we test them early on because for first-line therapy we want to know if they have these genetic alterations…The new guidelines advise testing when the person is first diagnosed…They recommend that clinical characteristics…should ***not*** be used in the selection criteria for testing. And the results should be available within two weeks of receiving the specimen, with the goal one week, though even in a place like ours, that is not always the case."

Ming Tsao, MD, a pathologist at the University of Toronto, cautioned that tumor tissue is limited. To make the best use of the tissue that is available, Dr. Tsao said EGFR testing could be done first, then ALK testing done only in EGFR-negative patients. He recommended using the most sensitive platforms available and warned that there are insufficient data at this point for doing immunohistochemistry for ALK.

Pranil Chandra, DO, a pathologist in Nashville TN, said that in his practice all non-squamous cell carcinomas get tested for EGFR and ALK, "There is enough of a predilection and a propensity for patients with early-stage disease to progress that we feel it is necessary to test all non-squamous cell lung cancer for EGFR. What happens is once a diagnosis is rendered by one of our 70 community-based pathologists…we have an algorithm where the pathologist orders EGFR and ALK testing up front. The tissue is sent to our central reference lab and processed further for ALK testing. We do the FDA-approved test for ALK. For EGFR we have a PCR-based test."

REGULATORY NEWS

CMS issues proposed IPPS for medtech DRGs

The proposed Inpatient Prospective Payment System (IPPS) rule for 2014, issued by CMS, includes a number of changes to Medicare payment rates for the nation's 3,400 acute care hospitals. Among the reimbursement changes for specific procedures are:

- Operating payments +0.8% for acute care hospitals (vs. +2.3% last year) that participate in the Inpatient Quality Reporting Program. Non-participating hospitals would have their payments cut by 2.0%. However, this includes a charge compression fix that may benefit hospitals.
- Heart valves +2.0% (vs. +0.8% last year).
- Implantable cardioverter-defibrillators (ICDs) +7.1%.
- Pacemakers +4.8%.
- Drug-eluting stents +2.6%.
- Lap-Band -2%.
- Neurostimulation +2.1%.
- Ventricular assist devices -0.2% (vs. +11.9% last year).
- Spinal fusions +6.2%.
- Artificial discs +6.1%.
- Hip and knee replacements +3.6%.
- Extremity replacements +7.4%.
- General surgery supplies +1.1%.
- Urology supplies +4.9%.

Long-term care hospital payments would increase 1.1%. Beginning in FY2014, CMS will implement the 25% patient threshold rule, under which long-term care hospitals that admit >25% of their patients from a single acute care hospital will get paid for the patients at a lower IPPS rate. In addition, CMS is seeking feedback on preliminary findings from research on criteria to identify patients who are chronically critically ill and medically complex, which are the patients CMS believes are the most appropriate core population for long-term care hospitals (and for full payment).

Beginning in 2015, CMS will implement a new **Hospital-Acquired Condition Reduction Program**. Hospitals that rank among the lowest-performing 25% with regard to hospital-acquired conditions will be paid 99% of what they would otherwise be paid under the IPPS.

CMS proposes FY2014 payments/policies for IRFs

CMS issued a proposed rule for Inpatient Rehabilitation Facilities (IRFs) and changes to its IRF Quality Reporting Program (QRP). Among the changes are:

- An overall increase of $150 million (2.0%) in aggregate payments to IRFs.
- A requirement that, for a facility to be excluded from the hospital IPPS, 60% of an inpatient hospital's patients must meet the specific criteria for ≥1 of 13 conditions.
- A new risk-adjusted measure of determining whether pressure ulcers are new or worsened.
- Three new quality measures: (1) percent of patients getting a flu shot, (2) vaccination of healthcare workers at the facility, and (3) all-cause readmission for 30 days.

Hydrocodone scheduling

If the FDA doesn't recommend the Drug Enforcement Administration (DEA) reschedule this opioid from a Schedule III to a Schedule II drug with tighter controls, and if the DEA doesn't do it on its own, perhaps a bill introduced by Sen. Charles Schumer (D-NY) will get it done. Schumer introduced the Safe Prescribing Act of 2013, which would mandate the change in scheduling.

FDA approvals/clearances

- **CSL BEHRING's Kcentra (prothrombin complex concentrate, human)**, which was developed to reverse the effects of warfarin, was approved. However, it does not reverse the effects of **Boehringer Ingelheim's Pradaxa** (dabigatran), **Johnson & Johnson** and **Bayer's Xarelto** (rivaroxaban), or **Bristol-Myers Squibb** and **Pfizer's Eliquis** (apixaban).
- **INTERVALVE's V8 balloon catheter**, which is designed for use in valvuloplasty or transcatheter aortic valve replacement, received 510(k) clearance.
- **JOHNSON & JOHNSON/DEPUY ORTHOPAEDICS' Ceramax Ceramic Total Hip System** – J&J received supplemental premarket approval for a 36 mm version of this hip replacement.
- **NOVOSOURCE's NovoKnee system**, a low-cost knee implant, was cleared for use.
- **RAPTOR PHARMACEUTICAL's Procysbi (cysteamine bitartrate delayed-release)** was approved to treat nephropathic cystinosis, a rare genetic condition affecting ~500 people in the U.S. and ~3,000 worldwide. It already had orphan drug status.
- **ROCHE/GENENTECH's Actemra (tocilizumab)** was approved to treat polyarticular juvenile idiopathic arthritis (PJIA), a rare form of arthritis.
- **SECOND SIGHT MEDICAL PRODUCTS' Argus II Retinal Prosthesis System**, the first bionic eye, was approved for use in patients with advanced retinitis pigmentosa.
- **SHIRE's Vyvanse (lisdexamfetamine dimesylate)** was approved for use as maintenance therapy for children and teenagers with attention-deficit/hyperactivity disorder (ADHD). It is the only ADHD drug with a maintenance indication.
- **SPINE WAVE's StaXx IB system**, an intervertebral body fusion system that uses PEEK spacer technology combined with bone graft chambers, was cleared for use.
- **TELEFLEX's Arrow VPS G4**, a vascular positioning device, was cleared for use to help identify the exact site of the lower one-third of the superior vena cava and cavo-atrial junction using micro-Doppler ultrasound combined with advanced algorithms and intravascular ECG.

FDA recalls/warnings

- **ALLERGAN's Botox (onabotulinumtoxinA)** – The FDA issued a warning to healthcare providers that fake versions of this toxin are being marketed in the U.S. under the brand names "Online Botox Pharmacy," "Onlinebotox.com," and "Onlinebotox" at a price much lower than legitimate Botox.
- **COVIDIEN/NEWPORT MEDICAL INSTRUMENTS' HT70 and HT70 Plus Ventilators Power Pac Batteries** – A Class I recall was initiated.
- **GLAXOSMITHKLINE and VALEANT PHARMACEUTICALS' Potiga (ezogabine)** – The FDA issued a safety warning that this anti-seizure medication can cause blue skin discoloration and eye abnormalities (pigment changes in the retina). The FDA said it does not know whether these changes are reversible and recommended that all patients taking Potiga have a baseline eye exam, followed by periodic eye exams.
- **HOSPIRA**
  - **Piperacillin + tazobactam** – Fifteen lots were voluntarily recalled due to the possibility of precipitation or crystallization in the IV bag or IV line when reconstituted.
  - **GemStar infusion system** was recalled (Class I) because of problems with the lithium battery.
- **MEDTRONIC's DBS** – The company issued an Urgent Medical Device Correction notice and has classified that communication as a Class I recall, warning that there was a risk of lead damage within the lead cap for this deep brain stimulation device.
- **OTSUKA PHARMACEUTICAL's Samsca (tolvaptan)** – The FDA issued a Drug Safety Communication, warning healthcare professionals and patients that this selective vasopressin V2-receptor antagonist intended for the treatment of clinically significant hypervolemic and euvolemic hyponatremia increased the risk of liver injury in a large recent trial in patients with autosomal dominant polycystic kidney disease (ADPKD). The FDA recommended stopping the drug if a patient develops signs of liver disease and limiting use to ≤30 days.

European regulatory news

- **Data confidentiality** – The General Court of the European Union issued a temporary injunction requiring the European Medicines Agency (EMA) to keep information from two drug companies – **AbbVie** and **InterMune** – confidential, which puts a crimp in the EMA's effort to make more clinical and non-clinical data available.
- **Italy** – National healthcare authorities seized ~268,000 medical devices, with an estimated value of $1.7 million, following inspections in 1Q13. The inspectors found that 19.3% of medical devices and 26.8% of pharmaceuticals examined in ~5,300 inspections were in violation of established standards.
- **ASTELLAS PHARMA and MEDIVATION's Xtandi (enzalutamide)** – The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended approval to treat metastatic castration-resistant prostate cancer (CRPC).
- **AXOGEN's AxoGuard Nerve Protector and AxoGuard Nerve Connector**, which are used in nerve repair, both received a CE Mark.
- **CELGENE's Revlimid (lenalidomide)** – CHMP recommended approval of this multiple myeloma drug to treat certain patients with myelodysplastic syndromes.
- **ROCHE/GENENTECH and CURIS' Erivedge (vismodegib, GDC-0449)** – CHMP recommended approval of this investigational therapy for advanced basal cell carcinoma.
- **ST. JUDE MEDICAL's Allure Quadra**, a cardiac resynchronization therapy (CRT) pacemaker with quadripolar lead, received a CE Mark.
- **SANOFI/GENZYME's MAC1** – CHMP recommended approval of this tissue-engineered treatment for cartilage defects.
- **Tetrazepam** – The EMA's risk-assessment committee recommended that the European Commission suspend use of all medications containing tetrazepam, a benzodiazepine approved to treat spasticity and back and neck pain, after it was linked to serious skin reactions.
- **VIVUS' Spedra (avanafil)** – CHMP recommended approval of this erectile dysfunction drug.

Regulatory news from other countries

- ***Brazil:*** A judge exempted the country's chief manufacturers of *in vitro* diagnostic equipment from inspections of their international facilities by Anvisa, the national health regulatory agency. The decision came in a challenge by Brazil's main IVD association over regulatory backlogs. Anvisa plans to appeal the decision.
- ***France:*** According to a story in ***Clinica***, France is now requiring that its healthcare authority review real-world data about pricing decisions for reimbursed drugs and devices, and that companies conduct stringent post-reimbursement studies to determine price-control levels. At present, the government uses cost-benefit studies by the country's independent health authority to set prices for reimbursed products. The government is also seeking to cut prices for generics by even more than previously through a "reference price" mechanism.
- ***India:*** The health ministry announced a new policy that will stop sales of any drugs that are banned by the European Union, the U.S., the U.K., Canada, Japan, or Australia, at least until clinical trials in India determine there is no safety issue.
- ***Israel:*** The Labor, Welfare, and Health Committee approved a law that imposes a fine on pharmas that do not include Arabic and Russian translations in their package information.
- ***Russia:*** Speaking at the BIO International Convention in Chicago, Sergey Tsyb of the Russian Ministry of Industry and Trade said the Russian government plans to establish six model "biopharma" centers, to encourage adherence by domestic pharmas to international good manufacturing practices, and to ensure that Russian pharmas control 50% of the market by 2020. He said the Russian pharma sales environment is healthy, "and we are open to collaboration."

2013 FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
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 Pharmaceuticals** 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