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 *detailed* coverage of the **FDA's Circulatory System Devices Advisory Committee** two-day meeting in Gaithersburg, MD, on the safety of peripheral use of paclitaxel-eluting stents and balloons.

Top news of the week (*read details in other sections of Quick Takes*)

✓ DAIICHI SANKYO's quizartinib was rejected by the FDA for treating AML.

✓ EXELIXIS and ROCHE's Cotellic (cobimetinib) + Tecentriq (atezolizumab) – This combination failed to beat Merck's Keytruda (pembrolizumab) in a Phase III trial in non-mutated melanoma.

✓ ICER found both of these therapies overpriced:

- JOHNSON & JOHNSON's Spravato (esketamine) for treatment-resistant depression.
- NOVARTIS' Mayzent (siponimod) for relapsing MS, including secondary progressive MS.

✓ Paclitaxel – An FDA advisory committee agreed there is a signal of increased mortality with paclitaxel DES and DCBs but recommended they stay on the market.

✓ PFIZER is buying Array BioPharma.

✓ REGENERON PHARMACEUTICALS and SANOFI's REGN-3500 failed to beat Dupixent (dupilumab) in a Phase II trial in moderate-to-severe asthma.

✓ VBI VACCINES' Sci-B-Vac, a hepatitis B vaccine, met the primary endpoint in a Phase III trial, but failed to show non-inferiority to **GlaxoSmithKline's Engerix-B**.

SHORT TAKES

■ ABBOTT's HeartMate PHP – Enrollment in the pivotal SHIELD-II trial of this percutaneous heart pump has resumed. *Remember, recruitment was halted twice.*

■ ABBVIE and ROCHE's Venclexta (venetoclax) – Analyses of the Phase III BELLINI trial, presented at the European Hematology Association (EHA) meeting in Amsterdam, Netherlands, suggest that overall the risk:benefit is not positive for this BCL2 inhibitor in multiple myeloma. While venetoclax significantly improved progression-free survival (PFS) – the primary endpoint – overall survival was worse vs. placebo (79% vs. 88%). However, the analyses also found subgroups that did significantly better [t(11;14) translocations] with the drug and other subgroups that did significantly worse (low BCL2 expression, high-risk cytogenetics, or ISS Stage III). *Remember, in March 2019 the FDA put a partial hold on venetoclax in multiple myeloma.*

- ALEXION PHARMACEUTICALS' Ultomiris (ravulizumab-cwvz) – A supplemental biologics license application (sBLA) was granted priority review by the FDA as a treatment for atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA). The PDUFA date is October 19, 2019.

- ARCTURUS THERAPEUTICS expanded its collaboration with Ultragenyx, getting the exclusive rights to collaborate on discovery and development of 12 rare disease targets.

- ASAHI KASEI/ZOLL MEDICAL bought TherOx, which gives it SuperSaturated Oxygen Therapy delivery systems.

- BIOMARIN's vosoritide (BMN-111) – A 35-patient, 4-year Phase II study, published in the ***New England Journal of Medicine***, found that this drug improved bone growth in children and teenagers with achondroplasia, a form of dwarfism, showing an average growth increase of 2.4 inches/year.

- BIO-TECHNE's ExoDx Prostate Intelliscore, a test for evaluating a man's risk of developing prostate cancer, was granted breakthrough device designation by the FDA.

- CANADY LIFE SCIENCES bought Endocontrol, a French firm that makes robotic-assisted technologies for laparoscopic and minimally-invasive surgery.

- CELYAD's CYAD-01 – Data from the Phase I THINK and DEPLETHINK trials, presented at EHA, showed that this CAR T agent had good safety and tolerability in relapsed/refractory acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), with an objective response rate of 31%.

- COGNIZANT bought Zenith Technologies, and the new biopharmaceuticals and medical device company will be known as Cognizant-Zenith Technologies.

- CYTEL is merging with Axio Research, a biostatistics company, creating the world's largest biometrics provider.

- DAIICHI SANKYO's quizartinib was rejected by the FDA as a treatment for AML patients with a FLT3 mutation, issuing a complete response letter.

- DR. REDDY'S LABORATORIES' Zembrace (sumatriptan) and Tosymra (sumatriptan nasal spray), both migraine treatments, are being sold to Upsher-Smith Laboratories.

- Ebola update – Uganda is taking an aggressive approach to addressing the spread of Ebola, approving use of:
  - Gilead Sciences' Remdesivir (GS-5734)
  - Mapp Biopharmaceutical's ZMapp
  - Regeneron Pharmaceuticals' REGN-EB3

- EDWARDS LIFESCIENCES' Pascal – In data presented at TVT in Chicago, off-label, compassionate use of this transcatheter mitral valve repair system to treat 28 patients with severe tricuspid regurgitation showed some success, reducing regurgitation severity and NYHA Class and increasing 6-minute walk test distances.

- EIGER BIOPHARMACEUTICALS' avexitide, an investigational treatment for post-bariatric hypoglycemia, was granted breakthrough therapy status by the FDA.

- ENANTA PHARMACEUTICALS' EDP-938 met the primary endpoint and a key secondary endpoint in a Phase IIa trial in respiratory syncytial virus (RSV), significantly reducing viral load and clinical symptoms vs. placebo.

- EXELIXIS and ROCHE's Cotellic (cobimetinib) + Tecentriq (atezolizumab) – This combination of a MEK inhibitor and a PD-L1 inhibitor missed the primary endpoint in the Phase III IMspire170 trial, failing to extend PFS more than Merck's Keytruda (pembrolizumab) alone in patients with untreated non-mutated melanoma.

- FFR – The unblinded, 918-patient MR-INFORM trial, published in the ***New England Journal of Medicine***, found that MRI was non-inferior to fractional flow reserve (FFR) and angiography for guiding revascularization in stable angina patients. However, the non-inferiority margin was so large (6%) that it raises questions about the findings. The composite of death, non-fatal MI, or target-vessel revascularization (TVR) at 1 year was 3.6% for MRI vs. 3.7% for FFR.

- Gabapentinoids **[e.g., Pfizer's Lyrica (pregabalin) or Neurontin (gabapentin)]** – A Swedish study, published in ***BMJ***, of nearly 200,000 people taking gabapentinoids found that patients (particularly younger people age 15-24) treated with these drugs for epilepsy, nerve pain, and anxiety disorders have a 26% increased risk of suicidal behavior, a 24% increased risk of unintentional overdose, a 22% increased risk of head/body injuries, and a 13% increased risk of road traffic incidents.

- GALDERMA LABORATORIES' Oracea (doxycycline) + Soolantra (ivermectin) – The results of the Phase IIIb/IV ANSWER trial, published in the ***Journal of the American Academy of Dermatology***, showed that this combination of an oral agent and a topical cream was significantly better than the topical cream (Soolantra) alone in reducing inflammatory rosacea lesions (-80.3% vs. -73.6%).

- GEL-E's Life Foam, an expanding, injectable hemostat for temporary bleeding control in patients with non-compressible abdominal wounds not suitable for a tourniquet in battlefield and trauma conditions, was granted breakthrough device designation by the FDA.

- GILEAD SCIENCES is collaborating with **Nurix Therapeutics** on development of novel therapies for cancer and other diseases.

- GLAUKOS is buying **DOSE Medical**, which develops drug delivery platforms for retinal disease treatment.

- IRONWOOD PHARMACEUTICALS and ALLERGAN's Linzess (linaclotide) – A Phase IIIb trial found that 29.7% of patients with irritable bowel syndrome with constipation (IBS-C) had a reduction in the composite of bloating, pain, and discomfort with Linzess vs. 18.3% with placebo. Linzess also met both secondary endpoints, significantly (and clinically meaningfully) improving overall abdominal symptoms.

- JAZZ PHARMACEUTICALS' Sunosi (solriamfetol), a dopamine + norepinephrine reuptake inhibitor for excessive daytime sleepiness, was given a Schedule IV designation by the Drug Enforcement Administration (DEA). This was the last hurdle before marketing could get underway.

- KYMERA THERAPEUTICS' KYM-001 – New preclinical data for this IRAK4 inhibitor, an oral protein degradation drug, in MYD88-driven lymphoma presented at the International Conference on Malignant Lymphoma in Lugano, Switzerland, showed early efficacy and safety.

- MELINTA THERAPEUTICS' Baxdela (delafloxacin), an antibiotic for treating community-acquired bacterial pneumonia, was granted priority review status by the FDA. The PDUFA date is October 24, 2019.

- MERCK MSD's Prevymis (letermovir) – The European Conference on Infections in Leukemia issued revised clinical practice guidelines, published in ***The Lancet Infectious Diseases***, on the use of letermovir to prevent cytomegalovirus in adults undergoing an allogeneic hematopoietic stem cell transplant.

- MERIT MEDICAL SYSTEMS bought **BrightWater Medical**, which makes the ConvertX system for treating severe ureteral obstructions.

- NOVARTIS' Mayzent (siponimod) – The Institute for Clinical and Economic Review (ICER) said the list price of $88,561 for this S1P1 receptor modulator for relapsing multiple sclerosis (MS), including active secondary progressive MS (SPMS) is "far out of line" compared to its benefits and recommended the company lower the price.

- NOVOCURE's Optune (tumor treating fields, TTF) – At a local coverage decision (LCD) meeting of the Durable Medical Equipment Medicare Administrative Contractors on criteria for coverage of this treatment for newly diagnosed glioblastoma, speakers expressed concern about continuity of care if coverage is restricted to National Comprehensive Cancer Network (NCCN) or National Cancer Institute (NCI) centers. Other concerns the speakers expressed included: a proposed requirement that Optune must be used 18 hours/day and a proposed requirement that treatment be started within 7 weeks of chemotherapy or radiation. Some speakers also urged the panel not to limit use to newly diagnosed patients.

- ONTERA was awarded a nearly $1 million contract by the Intelligence Advanced Research Projects Activity to develop a point-of-care Zika diagnostic test.

- Paclitaxel – The FDA's Circulatory System Devices Advisory Committee agreed unanimously that there is a signal of increased mortality with paclitaxel drug-eluting stents (DES) and drug-coated balloons (DCBs), but the devices should not be taken off the market. However, they said patients should be informed and make the final decision on use, and new studies should follow patients for at least 3-5 years.

- PAREXEL is collaborating with **CluePoints** on clinical trial and compliance work.

- PFIZER is buying **Array BioPharma**, which will give it Braftovi (encorafenib) and Mektovi (binimetinib), which in combination are used to treat $BRAF^{V600E/K}$+ unresectable/metastatic melanoma, and more.

- REGENERON PHARMACEUTICALS and SANOFI's REGN-3500 – In a 296-patient Phase II trial in moderate-to-severe asthma not well controlled with an inhaled corticosteroid (ICS) and a long-acting beta-agonist (LABA), this anti-IL-33 failed to beat Dupixent (dupilumab), and, in fact, Dupixent was numerically better. Combining REGN-3500 and Dupixent also failed to do better than Dupixent alone.

- UNITEDHEALTHCARE – The Federal Trade Commission cleared the purchase of **DaVita**, provided certain conditions are met, including divestiture of DaVita's HealthCare Partners of Nevada to Intermountain Healthcare, which, in turn, must divest its minority stake in P3 Health Partners.

- UNITY BIOTECHNOLOGY's UBX-0101 – Small, early-stage, multi-dose Phase I trials in osteoarthritis found this non-opioid pain drug was safe, with signs of efficacy in terms of improvement in pain and functional scores, but researchers said it is likely to need higher doses or more frequent administration.

- VALNEVA ended its partnership with **GlaxoSmithKline** on vaccine development.

- VBI VACCINES' Sci-B-Vac, a 2-dose hepatitis B vaccine, met the primary endpoint in a Phase III trial, with a sero-protection rate of 91.4% vs. 76.5% with GlaxoSmithKline's Engerix-B. However, Sci-B-Vac missed a key secondary end-point, failing to show non-inferiority to Engerix-B, a 3-dose vaccine, in patients age ≥18.

- VOYAGER THERAPEUTICS – **Sanofi** is giving up its options on the world-wide rights to VY-HTT01 for Huntington's disease and ex-U.S. rights to VY-FXN01 for Friedreich's ataxia. Sanofi also ended is alliance on spinal muscular atrophy (SMA).

NEWS IN BRIEF

BEIGENE

- In partnership with **SpringWorks**, launched a new biotech, **MapKure**. BeiGene is giving it BGB-3245, a BRAF inhibitor.

- Tislelizumab. Celgene gave its rights to this PD-1 inhibitor back to BeiGene.

BLUEBIRD BIO's Zynteglo (autologous CD34+ cells encoding βA-T87Q-globin gene)

The company said this gene therapy for beta-thalassemia, which was recently approved in Europe:

- Won't be launched there until 2020 because of manufacturing issues.

- Won't have to be paid in one lump sum €1.57 million (USD$1.8 million). Rather, the company is proposing a one-time payment of €315,000 and then yearly payments of €315,000 for 4 years – but only as long as the therapy continues to be effective.

JOHNSON & JOHNSON's Spravato (esketamine)

- **The good news:** A Phase III withdrawal study, published in ***JAMA Psychiatry***, found that patients with treatment-resistant depression who achieved remission with esketamine + an oral antidepressant had a significantly lower rate of relapse vs. an antidepressant alone. Patients who achieved stable response on esketamine/antidepressant also had significantly fewer relapses than an antidepressant alone.

- **The bad news:** In its final report, ICER concluded that this therapy for treatment-resistant depression (TRD) is not cost-effective at the current price ($32,400/year), and to be cost-effective would have to cost 25%-52% less ($17,700-$25,200/year).

ONCOPEPTIDES' Ygalo (melflufen)

In data presented at the EHA meeting:

- In the Phase I/II ANCHOR trial of a Ygalo triplet [+ dexamethasone + Johnson & Johnson's Darzalex (daratumumab) or Takeda's Velcade (bortezomib)] in relapsed/refractory multiple myeloma, among completers, there was a 100% overall response rate with the Velcade combination and 82% with the Darzalex combination. The median duration of treatment was 7.4 months with Velcade and 7.9 months with Darzalex. Both triplets were considered safe and tolerable.

- The O-12-M1 trial demonstrated that melflufen can stabilize disease in multiple myeloma patients between treatments.

Postmarketing trials

A study, published in ***BMC Medicine***, found that, of the 110 new drugs/biologics approved from 2009-2012:

- 55.5% had ≥1 postmarketing commitment (an FDA request for a postmarketing trial, not a mandate), including 33 requiring a new clinical trial.
- **The good news:** 90.3% of the requested trials were listed on www.clinicaltrials.gov, and 82.1% were listed as completed or terminated.
- **The bad news:** 81.8% of the studies were not completed on time, and the results of only 48.3% were ever published in peer-reviewed journals.

REGULATORY NEWS

Regulatory tidbits

- Biologics
  - Rep. Jan Schakowsky (D-IL) along with several other legislators introduced legislation – the Price Relief, Innovation, and Competition for Essential Drugs (PRICED) Act – that would reduce the market exclusivity for biologics from 12 years to 5 years.
  - The PRICED Act may get some support from a study, published in ***Nature Biotechnology***, that found the development time for biologics is similar to or even shorter than for small molecules.

- Bundled payments. The Centers for Medicare and Medicaid Services (CMS) said it will no longer exclude Medicare accountable care organizations (ACOs) from participating in Bundled Payments for Care Improvement (BPCI) advanced savings model, but providers participating in Model Year 3 (the highest downside risk) will take precedence over ACOs in the enhanced track that starts January 1, 2020.

- E-Prescribing. CMS issued a proposed rule that would update the electronic prescribing and prior authorization process for Medicare Part D to "reduce the time it takes for a patient to receive needed medications and ease the prescriber burden by giving clinicians the flexibility and choice to complete prior authorization transactions electronically."

- FDA advisory committees
  - **Calendar.** The FDA used to post on its website (www.fda.gov) the tentative dates for each of the various advisory committees. With the new website design, they have eliminated that. Now, only official, confirmed dates are posted. You may have thought you just couldn't find the tentative dates, but the FDA has confirmed that those dates are no longer available, so it is not your inability to find them; they just aren't there.
  - **Reduction.** President Trump issued an executive order that directs all federal agencies (which includes the FDA) to eliminate at least one-third of its current committees by September 30, 2019. Exactly how this will affect the FDA remains to be seen.

- Medical devices. The FDA's Center for Devices and Radiological Health (CDRH) is updating its medical device reporting (MDR) program, which monitors the safety of marketed devices. The Alternative Summary Reporting (ASR) program was ended, and MAUDE will be made more "user friendly."

- Opioids. The FDA issued draft guidance on risk:benefit assessment of opioids and withdrew its 2014 guidance. Among the recommendations in the new guidance are that companies provide information on:
  - Whether the new drug has any characteristics that would mitigate the risks of overdose, abuse, or addiction.
  - Whether their drugs have novel or greater risks vs. other marketed opioids on the market.
  - The public health implications of their products in terms of risks to non-patients.

- Valsartan contamination. A fourth potential carcinogen has been detected in lots of this antihypertensive drug. **Valisure**, an online pharmacy, found dimethylformamide (DMF) in batches it bought. The levels are not above FDA acceptable levels, so the company can't return the product and get a refund from the supplier, but Valisure also doesn't want to sell it. Valisure is so concerned that it filed a Citizen Petition with the FDA seeking to have the Agency lower the acceptable level of the agent.

FDA approvals/clearances

- AMAG PHARMACEUTICALS and PALATIN TECHNOLOGIES' Vyleesi (bremalanotide), a malanocortin-4 receptor agonist, was approved to treat hypoactive sexual desire disorder (low libido) in premenopausal women.

- APOLLO ENDOSURGERY's Orbera, an intragastric liquid-filled balloon system for treating obesity, was given labeling updates that include additional precautions, new adverse event tables, clarification of contraindications, and other procedure-related changes.

- AXONICS MODULATION TECHNOLOGIES' r-SNM – The FDA granted approval for full-body MRI scans in patients with this rechargeable sacral neuromodulation device in the ARTISAN-SNM pivotal trial for treating overactive bladder.

- CELERITY and BAXTER's Myxredlin (short-acting human insulin) was approved.

- COCHLEAR's Nucleus Profile Plus Implant, an MRI conditional (1.5 and 3.0 Tesla) cochlear implant system, was approved for treating hearing loss.

- JOHNSON & JOHNSON/ETHICON was granted 510(k) clearance for use of its airless spray devices to deliver Grifols' Vistaseal, a fibrin sealant for controlling surgical bleeding.

- MERCK MSD's Keytruda (pembrolizumab) was granted accelerated approval for use as a single-agent treatment of metastatic small cell lung cancer (SCLC) patients who progressed on/after platinum-based chemotherapy and ≥1 prior therapy.

- NOVO NORDISK's Victoza (liraglutide) was granted expanded approval for use in treating pediatric patients age ≥10 with Type 2 diabetes.

- PHILIPS' HeartStart OnSite and HeartStart Home, over-the counter-automated external defibrillators, were granted premarket approval (PMA), a new requirement the FDA imposed in 2015 even for already cleared devices.

- QUIDEL's Triage TOX Drug Screen, 94600, a fluorescence immunoassay test for simultaneous detection of drug metabolites in urine, was granted 510(k) clearance.

- VERTEX PHARMACEUTICALS' Symdeko (tezacaftor + ivacaftor) was granted expanded approval to treat cystic fibrosis patients age ≥6.

- ZEBRA MEDICAL VISION's HealthICH, an artificial, intelligence-powered algorithm for detecting intracranial hemorrhages, was granted 510(k) clearance.

FDA recalls/warnings

- COOK MEDICAL's Advance Enforcer 35 Focal-Force Percutaneous PTA Balloon Catheter 6 mm x 4 cm, for percutaneous transluminal angioplasty (PTA) of peripheral artery lesions, was recalled (Class I) because of multiple reports of balloons bursting below the rated burst pressure.
- EDWARDS LIFESCIENCES' IntraClude Intra-Aortic Occlusion Device – The company warned users about the risk of the device bursting during cardiopulmonary bypass, recommending that users exchange the device or change the operating strategy.
- GE HEALTHCARE's Giraffe Warmers and Panda iRes Warmers – The company issued a voluntary field corrective action because these hospital-use devices may crack, break, or become damaged if the units are not properly used.
- INFUSION OPTIONS is voluntarily recalling all lots of its sterile products due to sterility issues.
- PREMIER PHARMACY LABS is recalling all of its sterile drugs due to sterility issues.
- RXQ COMPOUNDING voluntarily recalled all of its sterile products and agreed to voluntarily cease production due to sterility issues.
- TELEFLEX MEDICAL's Hudson RCI Sheridan and Sheridan Endotracheal Tubes were recalled due to the risk of the connector disconnecting from the breathing circuit.
- VIDA INTERNATIONAL got a warning letter for violations (including inadequate drug testing) at its plant in Taoyuan City, Taiwan.

European Regulatory News

- *In vitro* diagnostics – The European Commission warned that there may be temporary shortages of some medical devices for health institutions, noting that "manufacturers may choose to stop the production of certain medical devices…if [devices] do not get their certificates on time."
- ASTRAZENECA and MERCK MSD's Lynparza (olaparib), a PARP inhibitor, was approved by the European Commission for front-line maintenance in BRCA+ ovarian cancer.
- BIOCORP's Mallya, a smart sensor for tracking the dose, date, and time of insulin injections in diabetics, was granted a CE Mark.
- GLUCOME's Decision Support System, a cloud-based algorithm-based software for facilitating personalized management of Type 2 diabetes, was granted a CE Mark.

U.K.'s National Institute for Health and Care Excellence (NICE) News

- ABBVIE's Humira (adalimumab) – NICE recommended use of this TNF inhibitor to treat uveitis.
- ALLERGAN's Ozurdex (dexamethasone implant) – NICE recommended use to treat uveitis.
- AMGEN's Blincyto (blinatumomab) – NICE recommended use in treating acute lymphoblastic leukemia (ALL) in patients in their first complete remission and with minimal residual disease activity ≥0.1%.

Regulatory news from other countries

- *Canada.* Off-label use. Health Canada issued new guidance requiring drug companies to answer a series of questions about a particular treatment before the agency will decide whether it needs an investigational drug designation for use in an off-label trial. Companies will have to detail the risks of off-label use, their reason for not considering the off-label use as a separate trial, and explain how the proposed use conforms to recognized/current medical practice.
- *Japan.*
  - ALEXION PHARMACEUTICALS' Ultomiris (ravulizumab) was approved by the Ministry of Health, Labour, and Welfare (MHLW) to treat adults with paroxysmal nocturnal hemoglobinuria.
  - ASTRAZENECA's Breztri Aerosphere (budesonide/glycopyrronium/formoterol fumarate, PT-010) was approved by the MHLW to treat chronic obstructive pulmonary disease (COPD).
  - ROCHE's Rozlytrek (entrectinib) was approved by the MHLW to treat NTRK+ advanced recurrent solid tumors.

2019 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
June 20	**Merck MSD's Keytruda** (pembrolizumab) for first-line treatment, in combination with Pfizer's Inlyta (axitinib) for advanced renal cell carcinoma	PDUFA date
June 21	**Glenmark Pharmaceuticals' Ryaltris** (olopatadine + mometasone furoate) for seasonal allergic rhinitis	PDUFA date *Extended from March 21*
June 21	**Agios' Tibsovo** (ivosidenib) for front-line IDH1+ acute myeloid leukemia (AML)	PDUFA date
June 25	**Acer Therapeutics' Edsivo** (celiprolol) to treat vascular Ehlers-Danlos syndrome	PDUFA date
June 26	**Sanofi** and **Regeneron Pharmaceuticals' Dupixent** (dupilumab), expanded approval to treat severe chronic rhinosinusitis with nasal polyps	PDUFA date
June 27	**Celgene's Revlimid** (lenalidomide) for relapsed/refractory follicular lymphoma	PDUFA date
June 28	**Alexion Pharmaceuticals' Soliris** (eculizumab) – expanded approval to include neuromyelitis optica spectrum disorder in patients with anti-aquaporin-4 antibodies	PDUFA date
July 6	**Karyopharm Therapeutics' selinexor** for relapsed/refractory multiple myeloma	PDUFA date *Extended by FDA from April 6*
July 12	Limited population pathway for **antibacterial and antifungal drugs**	FDA public meeting
July 15-16	Discussion of ***in vitro* diagnostics**	FDA public workshop
July 16	Discussion of alternative approaches in clinical investigations of new animal drugs	FDA public workshop by the Center for Veterinary Medicine
July 17	Second of 3 public meetings on electronic submission of adverse event reports to FAERS	FDA public meeting
July 23	**Biomarkers of neurotoxicity**	FDA workshop
July 25	**Boehringer Ingelheim's Ofev** (nintedanib) – expanded use to treat systemic sclerosis-associated interstitial lung disease	FDA's Arthritis Advisory Committee
July 26	Endpoints for drug development in **heart failure**	FDA public meeting
July 29-30	**Topical drug development** – evolution of science and regulatory policy	FDA public workshop
July 31	**Intra-Cellular Therapies' lumateperone** for schizophrenia	FDA's Psychopharmacologic Drugs Advisory Committee
August 3	**Daiichi Sankyo's pexidartinib** for treatment of tenosynovial giant cell tumor (TGCT)	PDUFA date
August 8	Discussion of development of **antiviral drugs** to treat adenoviral infection in immunocompromised patients	FDA public workshop
August 12	Discussion of individualized **drug dosing** in the real-world	FDA public workshop
August 14	**Galt Pharmaceuticals' Orphengesic Forte** (orphenadrine citrate + caffeine + aspirin), a non-opioid painkiller	PDUFA date
August 18	**Roche's entrectinib** for NTRK fusion-positive solid tumors and ROS1+ metastatic non-small cell lung cancer (NSCLC)	PDUFA date
August 29	**Nektar Therapeutics/Inheris Biopharma's NKTR-181** for low back pain	PDUFA date *Extended by the FDA from May 28*
September 3	**Celgene's fedratinib**, a JAK2 inhibitor for myelofibrosis	PDUFA date
Sept. 9-10	**Scientific computing**	FDA symposium
September 10	**Xeris Pharmaceuticals' Gvoke** (liquid glucagon autoinjection) for severe hypoglycemia	PDUFA date *Extended by the FDA from June 10*
September 17	Standards for future **opioid therapy approvals**	FDA public meeting
September 18	Implementing the FDA's **Predictive Toxicology Roadmap** – update	FDA public workshop
Sept. 24-26	**Regulatory science**	FDA global summit ***in Italy***
September 26	**Johnson & Johnson/Janssen's Darzalex (daratumumab)** in combination with VTD to treat multiple myeloma	PDUFA date
September 27	**Intra-Cellular Therapies' lumateperone** for schizophrenia	PDUFA date
September 28	**Amarin's Vascepa** (icosapent ethyl) – expanded approval to reduce cardiovascular risk in statin-managed patients with high triglycerides	PDUFA date

2019 FDA Advisory Committees and Other Regulatory Dates of Interest – continued (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
October 8	**Partners in Progress 2019:** Cancer patient advocates and FDA	FDA public workshop
October 19	**Alexion Pharmaceuticals' Ultomiris** (ravulizumab-cwvz) for treating atypical hemolytic uremic syndrome	PDUFA date
October 24	**Melinta Therapeutics' Baxdela** (delafloxacin) for community-acquired bacterial pneumonia	PDUFA date
November 4	**Roche's Xofluza** (baloxavir marboxil), expanded use as a single-dose treatment for patients at high risk of flu complications	PDUFA date
November 30	**Aquestive Therapeutics' Exservan** (riluzole oral film) for ALS	PDUFA date
December 4	**Celgene and Acceleron Pharma's luspatercept** for beta-thalassemia-associated anemia	PDUFA date
2020 FDA Advisory Committees and Other Regulatory Meetings and Events		
February 21	**Esperion Therapeutics' bempedoic acid** monotherapy to treat hypercholesterolemia	PDUFA date
February 26	**Esperion Therapeutics' bempedoic acid in combination with ezetimibe** to treat hypercholesterolemia	PDUFA date
March 25	**Celgene's ozanimod** (RPC-1063) for relapsing multiple sclerosis	PDUFA date
April 4	**Celgene and Acceleron Pharma's luspatercept** for myelodysplastic syndrome-associated anemia	PDUFA date