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 **American Academy of Orthopaedic Surgeons** (AAOS) meeting in Las Vegas and the **American College of Cardiology** (ACC) meeting in New Orleans.

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

- ✓ AMAG PHARMACEUTICALS' Makena (hydroxyprogesterone caproate) missed both primary endpoints in the confirmatory postmarketing trial endangering its accelerated approval for reduction of preterm birth.
- ✓ CELGENE's Abraxane (nab-paclitaxel) failed to improve disease-free survival in pancreatic cancer, though there was a small improvement in overall survival.
- ✓ FDA – The new (acting) commissioner is expected to be National Cancer Institute (NCI) Director Norman (Ned) Sharpless, MD.
- ✓ LILLY's Cyramza (ramucirumab) significantly extended PFS in a second Phase III trial in first-line EGFR+ metastatic NSCLC when added to erlotinib.
- ✓ Paclitaxel DCB and DES – The FDA's analysis found a 50% mortality risk at 5 years, and the Agency advised doctors not to use these devices if possible. The FDA plans to convene an advisory panel on the risk:benefit but has not yet set a date for that meeting.
- ✓ SMITH & NEPHEW is buying **Brainlab**'s joint reconstruction (orthopedic) business.

SHORT TAKES

- ABBVIE and **Principia Biopharma** mutually agreed to end their partnership on oral immunoproteasome inhibitors for treating inflammation and autoimmune disorders. Principia gets all rights to the program.
- ABIVAX's ABX-464 – The 6-month results from the maintenance part of a Phase IIa trial in ulcerative colitis patients were presented at the European Crohn's and Colitis Organisation meeting in Copenhagen, Denmark. The trial showed clinical remission at Week 8 35.0% vs. 11.1% (Nss, p=0.16) for placebo, a mucosal healing rate of 50.0% vs. 11.1% (p=0.034), and a per protocol clinical response rate of 70% vs. 33% (Nss, p=0.06).
- ACADIA PHARMACEUTICALS' Nuplazid (pimavanserin) – The U.S. Department of Justice is investigating marketing of this selective serotonin inverse agonist (SSIA) for Parkinson's disease.
- ALCYONE LIFESCIENCES' ThecaFlex DRx system, a delivery device with an intrathecal catheter and an implantable subcutaneous port for use in cerebrospinal fluid aspiration and therapy infusion, was granted breakthrough device status by the FDA.

- ALLERGAN's ubrogepant – The FDA accepted a new drug application (NDA) for review for this CGRP receptor antagonist as an oral treatment for acute migraine.

- AMAG PHARMACEUTICALS' Makena (hydroxyprogesterone caproate) missed both primary endpoints in the ~1,700-patient PROLONG postmarketing trial, failing to reduce the risk of preterm birth at <35 weeks and failing to meet the criteria for the neonatal morbidity and mortality composite index vs. placebo. Safety wasn't worse with Makena, and the rate of preterm births was significantly lower at Week 37 (but not at the key Week 35). *Makena's accelerated approval was contingent upon PROLONG being successful, so the FDA could revoke its approval.*

- ASTRAZENECA signed a 3-year collaboration with **Seres Therapeutics** on figuring out ways to utilize the microbiome to improve immuno-oncology.

- AXOVANT's AXO-AAV-GM2 – The company reported that an advanced Tay-Sachs disease infant was treated with this gene therapy. The 30-month-old baby did not deteriorate clinically or by MRI, as would have been expected, in the three months post-treatment. Production of functional β-Hexosaminidase A enzyme activity was reported, and the treatment appears to have been safe.

- BIOCARTIS' Idylla MSI – Biocartis is collaborating with **Bristol-Myers Squibb** on development and FDA clearance of this test for microsatellite instability as a companion diagnostic for immunotherapy of colorectal cancer.

- CELGENE's Abraxane (nab-paclitaxel) – added to Lilly's Gemzar (gemcitabine) – missed the primary endpoint in the pivotal 866-patient Phase III APACT trial in pancreatic cancer patients who had undergone surgical resection, failing to improve disease-free survival vs. Gemzar alone. However, there was a statistically significant (but small) improvement in overall survival with the addition of Abraxane.

- ESPERION THERAPEUTICS' bempedoic acid – At Week 12 of the 52-week Phase III CLEAR Harmony trial, published in the ***New England Journal of Medicine***, this oral small molecule added to maximum statin therapy significantly reduced LDL (-19.2 mg/dL vs. a -0.9 mg/dL with a statin alone). While there were no more serious adverse events with bempedoic acid (14.5% vs. 14.0%), more patients discontinued bempedoic acid for side effects (10.9% vs. 7.1%), though those side effects did not appear to be any worsening of statin side effects.

  The other more concerning finding: 0.4% of bempedoic acid patients vs. 0.1% of statin-only patients died from CV disease, and more bempedoic acid patients were hospitalized for heart failure (0.6% vs. 0.1%). Gout occurred more often with bempedoic acid (1.2% vs. 0.3%), and 30-day mortality after last dose was higher as well (0.9% vs. 0.3%).

- EXACTECH bought **XpandOrtho**, which makes knee replacement surgery instruments.

- GENERAL ELECTRIC/DATEX-OHMEDA was awarded a $100 million, 5-year contract by the U.S. Department of Defense to provide the military and federal civilian agencies with patient monitoring systems, accessories, and training.

- GENEURO's temelimab – The results of the Phase IIb ANGEL-MS extension study of this anti-HERV-W in multiple sclerosis were a little (repeat, little) better than the 1-year data, which failed to show any benefit. In the 2-year extension of the study, there was a reduction in brain atrophy and dose-dependent effects on disease progression by EDSS or the 25-foot timed walk.

- GILEAD SCIENCES' Descovy (emtricitabine + tenofovir alafenamide, TAF) met non-inferiority to Truvada (emtricitabine + tenofovir disoproxil fumarate) in the ~5,400-patient, 2-year, head-to-head Phase III DISCOVER trial in HIV pre-exposure prevention, with 7 Descovy patients vs. 15 Truvada patients developing an HIV infection. Descovy beat Truvada on bone and renal safety.

- HILL-ROM is buying **Voalte**, a mobile healthcare communications company.

- KARYOPHARM THERAPEUTICS' selinexor – The FDA extended its review of this XPO1 inhibitor for relapsed/refractory multiple myeloma by three months after the company responded to FDA questions by providing more data.

- LILLY's Cyramza (ramucirumab) met the primary endpoint in a second Phase III trial, RELAY, in first-line EGFR+ metastatic non-small cell lung cancer (NSCLC), significantly improving progression-free survival (PFS) vs. placebo when added to Roche's Tarceva (erlotinib).

- LIPOCINE's LPCN-1144 – In top-line results in a 16-week open-label, imaging trial in men with hypogonadism and non-alcoholic fatty liver disease (NAFLD), 48% of the 21 evaluable men had resolution of their NAFLD with this oral testosterone prodrug, and all of the men with NAFLD resolution had ≥35% liver fat reduction from baseline and an overall mean liver fat reduction of 55%.

- MERCK MSD's TICE BCG – Merck, the only supplier of this bladder cancer drug, said it is restricting shipments because of a shortage and will proportionally allocate available supplies to countries around the world based on their historical ordering averages.

- MERIT MEDICAL SYSTEMS' Rad Board – A study, published in ***Catheterization and Cardiovascular Interventions***, found that instead of reducing radiation exposure when used with a pelvic shield, this radial access arm board actually increased it, probably because of the "inability to use standard radiation shielding along with the Rad Board."

- NEUROCRINE BIOSCIENCES' NBI-74788 – In interim results from a Phase II trial in congenital adrenal hyperplasia, this corticotropin-releasing factor type 1 (CRF1) receptor antagonist significantly lowered levels of two hormones (17-OHP and ACTH) linked to the disorder in >50% of patients, exceeding the threshold for proof-of-concept.

- NORAMCO partnered with Nemus Bioscience, which will produce an analogue of cannabidiol with greater bioavailability (cannabidiol-valine-hemisuccinate, CBDVHS) for use in treating retinal diseases.

- NOVARTIS' Mayzent (siponimod) – The Institute for Clinical and Economic Review (ICER) released a draft evidence report on the effectiveness of this investigational treatment for secondary progressive multiple sclerosis (SPMS). ICER gave the drug a B+ rating for effectiveness in treating *active* SPMS, which means "high certainty of a small net health benefit" – a pretty high rating. For non-active SPMS, the rating was P/I ("promising but inconclusive").

- PENUMBRA's Penumbra – In the 270-patient COMPASS trial, published in ***The Lancet***, first-pass thrombectomy with this aspiration catheter met non-inferiority to a stent retriever (Medtronic's Solitaire) in terms of functional outcomes at 90 days in ischemic stroke patients. In addition, a cost-effectiveness analysis found that the Penumbra approach was $4,541-$5,074 cheaper. The investigators suggested this should change guidelines which currently recommend only stent retrievers, but the writers of an accompanying editorial weren't convinced that guidelines should change.

- PURDUE PHARMA's nalmefene Hcl, an investigational opioid antagonist for treating opioid overdoses that is longer acting than naloxone, was granted fast track status by the FDA. Purdue said it will *not* profit from the drug.

- SGLT2 inhibitors – An Australian study, published in ***The Journal of Clinical Endocrinology & Metabolism***, found that Type 2 diabetics taking an SGLT2 inhibitor have an increased risk of diabetic ketoacidosis during hospital admission (1.02 per 1,000 patients vs. 0.69 per 1,000 patients for non-users).

- SIEMENS HEALTHINEERS plans to integrate MRI Interventions' ClearPoint neuro-navigation system into its Access-I software application for the Magnetom line of MRI scanners. ClearPoint is expected to speed preplanning and data transfer.

- SPECTRUM PHARMACEUTICALS' Rolontis (eflapegrastim) – After the FDA asked for more manufacturing information, the company voluntarily withdrew its biologics license application (BLA) for this potential competitor for Amgen's Neulasta (pegfilgrastim), a treatment for chemotherapy-induced neutropenia.

- STEMLINE THERAPEUTICS licensed the exclusive global rights to SL-1001, a preclinical RET inhibitor, from **CRT Pioneer Fund**.

- STRYKER bought OrthoSpace, which makes biodegradable balloon devices for orthopedic applications, including a rotator cuff implant.

- SYNERON/CANDELA's Vbeam – A study, published in ***JAMA Dermatology***, found that this pulsed dye laser is safe and effective in treating birthmarks, port wine stains, and related vascular skin conditions on the face/body of infants and children.

- TAVR – Starting in mid-2019, the American College of Cardiology (ACC) will offer hospitals that perform transcatheter aortic valve replacement (TAVR) the ability to get Transcatheter Valve Certification through ACC.

- UCB's Cimzia (certolizumab pegol) met the primary endpoint in the 52-week, double-blind, 317-patient Phase III C-AXSPAND trial in adults with non-radiographic axial spondyloarthritis, with 47.2% of Cimzia patients having significant improvement in response on the ASDAS-MI vs. 7% of placebo patients. The results were published in the journal ***Arthritis & Rheumatology***. On the secondary endpoint of ASAS40, 47% of Cimzia vs. 11.4% of placebo patients achieved a 40% improvement at Week 12.

- ZAFGEN's ZGN-1258 – The company suspended plans to submit an investigational new drug (IND) application for this MetAP2 inhibitor to treat Prader-Willi syndrome after rat studies showed degeneration and other anomalies. The company said those issues were not observed in studies with its other MetAP2 inhibitors.

Very early research news

- Inflammatory bowel disease (IBD) – A mouse study by researchers at Washington University School of Medicine, published in ***Science Translational Medicine***, suggests a possible new target for treating IBD – a SERPINE-1 inhibitor.

NEWS IN BRIEF

EDWARDS LIFESCIENCES

- Invested in **Corvia Medical**, which has the InterAtrial Shunt Device – the first transcatheter device for treating heart failure with preserved ejection fraction (HFpEF). Edwards got the exclusive rights to acquire the company in the future.
- Bought undisclosed assets from **Mitralign**, which is developing an annuloplasty system for treating functional mitral and tricuspid regurgitation.

SMITH & NEPHEW

The company is buying

- **Brainlab**'s joint reconstruction business and will absorb the Brainlab sales force into its robotics sales force.
- **Osiris Therapeutics**, a regenerative medicine company.

TAKEDA

- **Entyvio (vedolizumab)** beat AbbVie's Humira (adalimumab) in the head-to-head Phase IIIb VARSITY trial of these two biologics in ulcerative colitis, with a 31.3% remission rate for Entyvio vs. 22.5% for Humira at Week 52.
- **SHIRE's Advate (Factor VIII, recombinant).** A Japanese study, published in the ***International Journal of Hematology***, found Advate was well tolerated and effective in treating hemophilia A patients. The data suggested it is better as a preventive therapy than used on-demand.

REGULATORY NEWS

Regulatory tidbits

- **FDA Commissioner.** When **Scott Gottlieb**, MD, leaves the post in early April 2019, Health and Human Services (HHS) Secretary Alex Azar said National Cancer Institute (NCI) Director **Norman (Ned) Sharpless, MD**, will become the acting FDA Commissioner while a search for a permanent head is underway – and that search has already begun. However, Dr. Gottlieb reportedly thinks Dr. Sharpless should get the job permanently.

  Dr. Sharpless is a graduate of the University of North Carolina School of Medicine, did a residency in internal medicine at Massachusetts General Hospital, and spent 2 years in a hematology-oncology fellowship at Harvard Medical School's Dana-Farber/Partners Cancer Care before joining UNC, where he ran the Lineberger Comprehensive Cancer Center. He's been the director of the NCI since 2017. He also co-founded two biotech companies, G1 Therapeutics and Sapere Bio.

  Dr. Sharpless appears to be on the same page as Dr. Gottlieb on the need for tighter regulation of **tobacco** and on limiting underage **vaping**.

  NCI Deputy Director Douglas Lowy will head the NCI while Dr. Sharpless is over at FDA.

- **Budgets.** President Trump's proposed fiscal year 2020 budget includes:
  - National Institutes of Health (NIH) **down 13%** to $34.4 billion.
  - Centers for Medicare and Medicaid Services (CMS) **down 4%** to $6.3 billion.
  - Office of the National Coordinator for Health Information Technology **down 28%** to $43 *million*.
  - FDA **up 12%** to $6.1 billion, including an additional $98 million for the Center for Devices and Radiological Health (CDRH) for cybersecurity, device safety, device reviews, and innovation.
  - Centers for Disease Control and Prevention (CDC) **down 1%** to $12 billion.
- **Cancer trials.** The FDA released five guidances (1 final, 4 draft) on clinical trial eligibility:
  - Enrolling adolescents in adult trials (final).
  - Minimum age for pediatric trials.
  - Patients with HIV, hepatitis B, or hepatitis C.
  - Patients with organ dysfunction or prior or current malignancies.
  - Patients with brain metastases.
- **Clinical trial design.** FDA Commissioner Dr. Gottlieb was critical of sponsors and contract research organizations for continuing to be reluctant to rethink clinical trial approaches.
- **Medical devices.**
  - **Metal.** The FDA is concerned about the level of risk from materials being used in implantable/insertable medical devices in terms of adverse/allergic reactions among small groups of patients, with the reactions sometimes occurring late (even years later).

    In particular, the Agency is looking at: breast implants, metals used in implants, nitinol, metal-on-metal hips, and more. The FDA is to release a white paper summarizing

the current scientific knowledge of metal implants and, in the fall, hold an advisory committee meeting to discuss the safety of nitinol and other metals in devices in patients with "hypersensitivity" reactions to metals.

- **Animal materials.** The FDA also is interested in ways to improve the safety of devices made from animal-derived materials (e.g., additives in device coatings or porcine heart valves). The Agency just issued final guidance in this area, with recommendations on how to minimize the risk of transmitting rare but serious infectious diseases.
- **New materials.** The Agency is studying new materials – e.g., graphene – and nanoparticles that are starting to be used in medical devices.

■ Medicare Part D spending.

The 11 drugs on which Medicare Part D spent the most money in 2017 are listed in this table.

Medicare Part D Drugs	
Drug	**Part D spending in billions in 2017**
Celgene's Revlimid (lenalidomide)	$3.31
Bristol-Myers Squibb and Pfizer's Eliquis (apixaban)	$3.08
Merck MSD's Januvia (sitagliptin)	$2.79
Sanofi's Lantus Solostar (insulin glargine)	$2.63
Johnson & Johnson's Xarelto (rivaroxaban)	$2.61
Gilead Sciences' Harvoni (sofosbuvir + ledipasvir)	$2.56
Pfizer's Lyrica (pregabalin)	$2.52
GlaxoSmithKline's Advair Diskus (fluticasone + salmeterol)	$2.37
AbbVie's Humira Pen (adalimumab)	$2.02
Boehringer Ingelheim's Spiriva (tiotropium bromide)	$1.66
Sanofi's Lantus (insulin glargine)	$1.55

■ Post-acute care. The Medicare Payment Advisory Commission (MedPAC) said a future unified payment model for post-acute care facilities should be based on an individual patient's stay, not the entire episode of care. MedPAC said an analysis found that an episode-based approach might influence providers to discharge patients too quickly. HHS and an outside vendor are working on a proposal for a unified post-acute care payment system, but it isn't expected to be submitted to Congress until 2022.

FDA approvals/clearances

■ ABBOTT's MitraClip was granted expanded approval to include treatment of patients with normal mitral valves who develop heart failure symptoms and have moderate-to-severe/severe functional mitral regurgitation (FMR).

■ AERIE PHARMACEUTICALS' Rocklatan (netarsudil + latanoprost) was approved to reduce intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

■ ALKEM LABORATORIES' generic valsartan was found not to be contaminated with NDEA or NDMA and was approved for use.

■ EXACTECH's Alteon Cup and XLE Liner acetabular system were cleared for use in the Alteon Platform.

■ INTUITIVE SURGICAL's da Vinci SP robot was granted expanded clearance for use in transoral otolaryngology robotic surgery (TORS) procedures in adults – for radical tonsillectomy (lateral oropharyngectomy procedures) and tongue base resection of tumors localized in the mouth, throat, or voice box.

■ NVISION BIOMEDICAL TECHNOLOGIES' Vector Hammertoe Correction System, a bio-implant for the foot and ankle, was cleared for use.

■ PFIZER's Trazimera (trastuzumab-qyyp, PF-05280014), a biosimilar of Roche's Herceptin, was approved to treat patients with HER2+ breast, gastric, or gastroesophageal junction cancer. Now, there are 4 biosimilars of Herceptin.

■ PURDUE PHARMA/ADLON THERAPEUTICS' Adhansia XR (methylphenidate HCl extended-release) was approved to treat attention-deficit/hyperactivity disorder (ADHD) for patients age ≥6, but it was given a boxed warning about the potential for abuse and dependence.

■ SANOFI and REGENERON PHARMACEUTICALS' Dupixent (dupilumab) was granted expanded approval to include treatment of adolescents age 12-17 with moderate-to-severe atopic dermatitis.

■ SONAVEX's EchoSure, a system that provides automated blood flow monitoring after vascular surgery, was granted 510(k) clearance.

■ THORNHILL RESEARCH's ClearMate was granted clearance through the de novo pathway to treat patients in the emergency room who have carbon monoxide poisoning.

FDA recalls/warnings

■ BIOCON received a Form 483 over contamination and data issues.

■ LUPIN's plant in Mandideep, India, was barred from getting new approvals for exports to the U.S. because of failure to resolve issues in warning letters.

■ Paclitaxel drug-coated balloons (DCBs) and drug-eluting stents (DES) for the periphery – The FDA updated its MedWatch Safety Alert about these devices, saying that its investigations found that at 5 years there was a 50% higher risk of death vs. control (20.1% vs. 13.4%) in patients getting these devices for femoropopliteal artery disease.

The FDA suggested that other treatment options should be used until more data are available, but didn't ban the devices. The FDA said it has identified a "potentially concerning signal of increased long-term mortality" with the devices in a pooled analysis of 3 studies with 5-year follow-up. The FDA plans to hold a meeting of its Circulatory Systems Devices Advisory Committee to discuss this and to re-examine the risk:benefit profile.

- PFIZER/HOSPIRA's sterile injectables plant in Irungattukottai, India, got a Form 483. However, the plant was already scheduled for closure.
- STOKES HEALTHCARE's pilocarpine ophthalmic solution – One lot was recalled due to a higher than typical level of a preservative.

European Regulatory News

- ***France and the U.K.*** Paclitaxel – Regulators in both these countries have begun their own investigations into the safety of paclitaxel devices for PAD. In the U.K., the Medicines and Healthcare products Regulatory Agency (MHRA) appointed an independent expert advisory group to investigate the safety of the devices. But the devices are not being taken off the market – yet.
- ***Germany.*** The government is partnering with **CARB-X** to spur development of antibiotics to fight drug-resistant bacteria (superbugs).
- ***Netherlands.*** Pharmacists at Erasmus Medical Center, the Amsterdam University Medical Center, and the Transvaal Pharmacy in The Hague are **compounding** some rare-disease drugs that are too expensive for patients.
- ADMEDUS' VascuCel, a collagen bioscaffold for use in vascular surgical procedures, was granted a CE Mark.
- BOSTON SCIENTIFIC's Watchman FLX, a next-generation left atrial appendage closure device, was granted a CE Mark to reduce the risk of stroke in patients with non-valvular atrial fibrillation.
- CELGENE's ozanimod was submitted to the European Medicines Agency (EMA) as a treatment for relapsing-remitting multiple sclerosis.
- MERCK KGAA and PFIZER's Bavencio (avelumab) – The EMA accepted this PD-L1 inhibitor for review as a treatment for advanced renal cell carcinoma (RCC) in combination with Pfizer's Inlyta (axitinib).
- MERCK MSD's Keytruda (pembrolizumab), an anti-PD-1, was granted expanded approval for use in combination with carboplatin and paclitaxel or Celgene's Abraxane (nab-paclitaxel) as a first-line treatment for metastatic squamous NSCLC.
- ORTHO CLINICAL DIAGNOSTICS' Vitros XT MicroSlide, a multi-test platform which allows laboratories to run two *in vitro* diagnostic tests simultaneously on one slide, was granted a CE Mark.
- PERSONAL GENOME DIAGNOSTICS' PGDx Elio Plasma Resolve, a liquid biopsy test for detecting microsatellite instability from plasma in cancer patients, was granted a CE Mark.
- REGENERON PHARMACEUTICALS and SANOFI's Praluent (alirocumab), a PCSK9 inhibitor, was granted expanded approval by the European Commission for reduction of cardiovascular (CV) risk in adults with atherosclerotic CV disease (ASCVD).
- REPROCELL is partnering with **Medicines Discovery Catapult** on accelerating drug development.
- ROCHE
  - Hemlibra (emicizumab) was approved by the European Commission to prevent bleeding episodes in hemophilia A patients without Factor VIII inhibitors.
  - MabThera (rituximab, Rituxan) was granted expanded approval by the European Commission to treat pemphigus vulgaris, a rare autoimmune disease.
- VOLUNTIS' Insulia, an updated software app that makes insulin dose recommendations for adult Type 2 diabetics via a smartphone or computer – and which allows doctors to monitor patient progress – was granted a CE Mark.

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

- JOHNSON & JOHNSON's Darzalex (daratumumab) – NICE reversed itself and is now recommending second-line use in combination with Takeda's Velcade (bortezomib) and dexamethasone in multiple myeloma, with the recom-mendation that funding be through the Cancer Drugs Fund.

Regulatory news from other countries

- ***China.***
  - CSTONE PHARMACEUTICALS' CS-3003 – The National Medical Products Administration (NMPA) approved the start of a clinical trial of this HDAC6 inhibitor in multiple myeloma.
  - HITGEN is collaborating with **Sun Pharma** to identify small molecule leads.

■ *Japan.*

- AKEBIA THERAPEUTICS' vadadustat (AKB-6548) – Akebia and Mitsubishi Tanabe Pharma Corp. (MTPC) agreed to collaborate on development and commercialization of this oral treatment for anemia related to chronic kidney disease (CKD) in Japan and certain other countries in Asia.
- NOVO NORDISK partnered with **Health2Sync** and will help promote Health2Sync's digital diabetes management app in Japan.

■ *South Korea.*

- ASLAN PHARMACEUTICALS' ASLAN-003 – The Korean rights to this DHODH inhibitor were licensed to **Bio-Genetics** for all indications, starting with acute myeloid leukemia (AML).
- RESMED bought **HB Healthcare**, a South Korean home healthcare equipment supplier.

2019 FDA Advisory Committees and Other Regulatory Meetings of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
tba	**Bausch Health's Duobrii** (halobetasol propionate + tazarotene) for psoriasis	PDUFA date – *FDA delayed February 15 decision by "a little"*
March tba	**Novartis' Mayzent** (siponimod, BAF-312) for secondary progressive multiple sclerosis	PDUFA date
March 18	**Roche's Tecentriq** (atezolizumab) for first-line treatment of extensive-stage small cell lung cancer in combination with carboplatin and etoposide	PDUFA date
March 19	**Sage Therapeutics' Zulresso** (IV brexanolone, SAGE-547) for postpartum depression	PDUFA date – *Review extended by 3 months from December 19, 2018*
March 20	**Jazz Pharmaceuticals' solriamfetol** (JZP-110) for excessive sleepiness in patients with narcolepsy or sleep apnea	PDUFA date – *Review extended by 3 months from December 20, 2018*
March 20	Strategies to reduce the risk of **Zika virus transmission**	FDA's Blood Products Advisory Committee
March 21	Discussion of **blood donations** by men who have sex with men	FDA's Blood Products Advisory Committee
March 21	**Glenmark Pharmaceuticals' Ryaltris** (olopatadine + mometasone furoate) for seasonal allergic rhinitis	PDUFA date
March 21	**Neuronix's NeuroAD Therapy System** for concurrent neurostimulation and cognitive training to treat mild-to-moderate Alzheimer's dementia	FDA's Neurological Devices Advisory Committee
March 22	**Sedor Pharmaceuticals' IM/IV Captisol-Enable Fosphenytoin** (fosphenytoin sodium and sulfobutylether beta-cyclodextrin sodium for injection) to treat generalized tonic-clonic status epilepticus and seizures during neurosurgery	PDUFA date
March 22	**Sanofi** and **Lexicon Pharmaceuticals' Zynquista** (sotagliflozin) – expanded approval of this SGLT2 inhibitor to include Type 1 diabetes	PDUFA date
March 23	**Palatin Technologies' bremelanotide** for hypoactive sexual desire	PDUFA date
March 24	**Recro Pharma's IV meloxicam** for acute pain after bunionectomy	PDUFA date
March 25-26	Discussion of **safety of breast implants**	FDA's General and Plastic Surgery Devices Advisory Committee
March 27	**AllerQuest's PRE-PEN Plus** for detecting IgE sensitization to penicillin antigens to rule out life-threatening penicillin allergic reactions	FDA's Pulmonary-Allergy Drugs Advisory Committee
April 1	**Evoke Pharma's Gimoti** (metoclopramide, EVK-001) for diabetic gastroparesis	PDUFA date *(not expected to be met)*
April 3	**Pharmacy benefit managers** (PBMs) – Cigna, CVS, Humana, United-Healthcare/OptumRx, and Prime Therapeutics – to discuss drug pricing	Senate Finance Committee hearing
April 3-5	**Sentinel Initiative** 5-year plan	FDA public workshop
April 6	**Karyopharm Therapeutics' selinexor** for relapsed/refractory multiple myeloma	PDUFA date ***Extended by FDA for 3 months to July 6***
April 11	**Merck MSD's Keytruda** (pembrolizumab) as monotherapy for first-line treatment for locally advanced/metastatic NSCLC in patients PD-L1+ ≥1% without EGFR or ALK mutations	PDUFA date
April 28	**Regeneron Pharmaceuticals** and **Sanofi's Praluent** (alirocumab) label claim for cardiovascular risk reduction	PDUFA date
April 30	**Heron Therapeutics' HTX-011** (bupivacaine + meloxicam) for postoperative pain	PDUFA date
May 1	**Sanofi Pasteur's Dengvaxia** for dengue fever	PDUFA date
May 13	**Regeneron Pharmaceuticals** and **Bayer's Eylea** (aflibercept) expanded approval to treat diabetic retinopathy	PDUFA date
May 21	Discussion of FDA's proposed rule changes for **outsourcing facilities and compounding pharmacies**	FDA public meeting
May 24	**Incyte's Jakafi** (ruxolitinib) for graft-versus-host disease	PDUFA date *Extended by the FDA from February 24*
June 10	**Xeris Pharmaceuticals' liquid glucagon autoinjector** for severe hypoglycemia	PDUFA date
June 10	**Merck MSD's Keytruda** (pembrolizumab) for first-line treatment, as monotherapy or in combination with chemotherapy, for recurrent/metastatic squamous cell head and neck cancer	PDUFA date
June 17	**Merck MSD's Keytruda** (pembrolizumab) for monotherapy of ≥3-line advanced SCLC	PDUFA date

2019 FDA Advisory Committees and Other Regulatory Meetings – continued (*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 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 28	**Alexion Pharmaceuticals' Soliris** (eculizumab) – expanded approval to include neuromyelitis optica spectrum disorder in patients with anti-aquaporin-4 antibodies	PDUFA date
June 30	**Nabriva Therapeutics' Contepo** (fosfomycin) for complicated urinary tract infections	PDUFA date
July 6	**Karyopharm Therapeutics' selinexor** for relapsed/refractory multiple myeloma	PDUFA date ***Extended by FDA from April 6***
August 3	**Daiichi Sankyo's pexidartinib** for treatment of tenosynovial giant cell tumor (TGCT)	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 19	**Roche's polatuzumab vedotin** for relapsed/refractory DLBCL	PDUFA date
September tba	**Lilly's Emgality** (galcanezumab-gnlm), expanded approval of this CGRP inhibitor to treat episodic cluster headaches	PDUFA date
September 3	**Celgene's fedratinib**, a JAK2 inhibitor for myelofibrosis	PDUFA date
September 27	**Intra-Cellular Therapies' lumateperone** for schizophrenia	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