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 advisory committee review of **Nektar Therapeutics' Kyvoda** (NKTR-181, oxycodegol), which provides some insight into the issues that likely will face all opioids coming before the FDA in the near future.

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

✓ The new Chinese **coronavirus** was detected in Japan and Thailand, and the CDC and CBP started screening airline passengers arriving from Wuhan, China, at LAX, SFO, and JFK airports.

✓ Paclitaxel – A new meta-analysis found an increased risk of all-cause death and major amputation for balloons used to treat chronic limb ischemia below-the-knee.

✓ **New safety issues:**

- EISAI's Belviq (lorcaserin) – The FDA warned that this obesity drug may be associated with an increased cancer risk.
- LEO PHARMA's Picato (ingenol mebutate) – The EMA's PRAC is reviewing this actinic keratosis gel over a possible link to skin cancer.

✓ **FDA advisory committees:**

- Rejected NEKTAR THERAPEUTICS' Kyvoda (NKTR-181, oxycodegol) for low back pain.
- Split on ESTEVE PHARMACEUTICALS' tramadol/celecoxib for acute pain.
- Rejected 24-2 INTELLIPHARMACEUTICS' Aximris XR (abuse-deterrent oxycodone ER) for severe pain.
- Split on DURECT's Posimir (bupivacaine ER), a non-opioid, for post-surgical pain.

✓ **The positive trial data:**

- ABBVIE's Skyrizi (risankizumab) beat Novartis' Cosentyx (secukinumab) in a head-to-head trial in psoriasis.
- BAYER's osocimab (BAY-1213790), a Factor XIa inhibitor, beat enoxaparin in a Phase II trial in VTE prevention.
- BIOFRONTERA's Ameluz (aminolevulinic acid HCl gel) in a Phase III trial with PDT in treating actinic keratosis.
- BRISTOL-MYERS SQUIBB's Sprycel (dasatinib) beat Novartis' Gleevec (imatinib) on survival in children with ALL in a head-to-head trial.

✓ **The negative trial data:**

- ACASTI PHARMA's CaPre (omega-3 phospholipid), a fish oil, in a Phase III trial in hypertriglyceridemia.
- ASTRAZENECA's Epanova (omega-3 carboxylic acids), another fish oil, in a Phase III CV outcomes trial.

SHORT TAKES

- ABBOTT's MitraClip – The FDA gave approval for the start of a 500-patient trial in patients with primary mitral regurgitation who are eligible for open-heart surgery, comparing this device to open-heart mitral valve surgical repair.
- ABBVIE's Skyrizi (risankizumab) – In a head-to-head, 327-patient, 52-week trial in moderate-to-severe psoriasis, this IL-23 antagonist beat Novartis' Cosentyx (secukinumab), an IL-17 inhibitor, on the primary and secondary endpoints. PASI-90 was achieved by 87% of Skyrizi patients vs. 57% of Cosentyx patients at 52 weeks.
- ACASTI PHARMA's CaPre (omega-3 phospholipid) missed the primary endpoint in top-line data from the Phase III TRILOGY-1 trial in patients with hypertriglyceridemia on statin therapy, failing to significantly reduce triglyceride levels vs. placebo (-30.5% vs. -27.5%) at Week 12. The company blamed a larger-than-expected placebo response.
- ANI PHARMACEUTICALS bought 23 generic products from Amerigen Pharmaceuticals.
- ASTELLAS/UNIVERSAL CELLS is collaborating with Adaptimmune Therapeutics on co-development and co-commercialization of stem-cell-derived allogeneic T cell therapies for cancer.
- ASTRAZENECA's Epanova (omega-3 carboxylic acids) – After an interim analysis of the 13,086-patient, global Phase III STRENGTH trial, a cardiovascular outcomes trial of this fish oil added to optimal statin therapy in patients with dyslipidemia and a high risk for cardiovascular disease, the trial was halted for futility.
- BAYER's osocimab (BAY-1213790) – The results of the 813-patient Phase II FOXTROT trial in patients undergoing knee arthroplasty, published in ***JAMA***, showed that a 0.3 mg/kg dose of this Factor XIa inhibitor, given postoperatively, was non-inferior in preventing venous thromboembolism (VTE) vs. enoxaparin and a 1.8 mg/kg dose was superior to enoxaparin.
- BIOFRONTERA's Ameluz (aminolevulinic acid HCl gel) – In follow-up 12-month results from a 50-patient Phase III trial of photodynamic therapy with Ameluz and the BF-Rhodo-LED lamp in treating actinic keratosis (AK) on the extremities, trunk and neck, overall lesion recurrence was 14.1% with Ameluz vs. 27.4% with placebo, meeting the criteria for superiority.
- BIOGEN bought **Pfizer's PF-05251749**, an early-stage CK-1 inhibitor, for use in treating behavioral and neurologic symptoms in psychiatric and neurologic diseases, starting with Sundowning in Alzheimer's disease and irregular sleep wake rhythm disorder in Parkinson's disease.
- BIOMARIN PHARMACEUTICAL's Valrox (valoctocogene roxaparvovec) – The company reportedly is considering pricing this gene therapy for hemophilia at $2-$3 million.
- BIONTECH is buying Neon Therapeutics for $67 million in stock.
- CLOVIS ONCOLOGY's Rubraca (rucaparib) – The FDA accepted a supplemental new drug application (sNDA) for this PARP inhibitor and granted priority review as monotherapy for BRCA1/2 mutant recurrent metastatic castrate-resistant prostate cancer. The PDUFA date is May 15, 2020.
- DARÉ BIOSCIENCE's Ovaprene – **Bayer** licensed the U.S. rights to this investigational hormone-free monthly contraceptive vaginal ring.
- DEXCOM is collaborating with Livongo Health to sync readings from its continuous glucose monitors with Livongo's digital health service, which analyzes data and provides personalized, real-time health information and coaching to the user's smartphone.
- DURECT's Posimir (bupivacaine extended-release) – The FDA's Anesthetic and Analgesic Drug Products Advisory Committee was evenly divided (6-6) on approval of this non-opioid painkiller for post-surgical pain.
- Ebola update – According to an update from Doctors Without Borders, the Ebola outbreak in the Democratic Republic of Congo is now the second-largest Ebola epidemic, with 3,388 cases and 2,233 people dead, and it is still not under control even though WHO declared it a public health emergency of international concern in July 2019.
- Electronic health records (EHRs) – A study, published in ***Annals of Internal Medicine***, found that, on average, physicians spend 16 minutes and 14 seconds using an EHR for each patient encounter.

- EPIC SYSTEMS, a large electronic health record (EHR) provider, is advising customers that it will stop working with (integrating) Google Cloud and instead focus on Amazon Web Services and Microsoft Azure. The reason: Epic said there wasn't sufficient interest in Google Cloud among its health system customers.

- ESTEVE PHARMACEUTICALS' tramadol 44 mg + celecoxib 56 mg – The FDA's Anesthetic and Analgesic Drug Products Advisory Committee, meeting jointly with the Drug Safety and Risk Management Advisory Committee, was evenly split 13-13 on approval of this opioid for treating acute pain.

- GALAPAGOS expanded its collaboration with Fibrocor Therapeutics, exclusively in-licensing 4 additional undisclosed fibrosis programs.

- GENETX BIOTHERAPEUTICS and ULTRAGENYX PHARMACEUTICAL's GTX-102 – The FDA approved an investigational new drug (IND) application, clearing the way for a Phase I/II trial of this antisense oligonucleotide in a trial in Angelman syndrome (AS).

- HIKMA formed an exclusive collaboration with Arecor to use its Arestat formulation technology in development of an undisclosed injectable for an undisclosed indication.

- HORIZON DISCOVERY GROUP signed a collaboration and licensing agreement to use Mammoth Biosciences' CRISPR platform on development of next-generation engineered CHO cell lines for use in biotherapeutics production (e.g., therapeutic antibodies).

- INTELLIPHARMACEUTICS' Aximris XR (abuse-deterrent oxycodone extended-release) – FDA's Anesthetic and Analgesic Drug Products Advisory Committee, meeting jointly with the Drug Safety and Risk Management Advisory Committee, voted 24-2 ***against*** approval of this opioid, which had been resubmitted to the FDA to manage pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which no alternative treatment is adequate.

- MASIMO is buying NantHealth's connected care business, which will give it DCX device connectivity, VCX patient vitals software, the HBox connectivity hub, and the Shuttle interface cable.

- MORPHOSYS' tafasitamab, an anti-CD19, was licensed to Incyte. The companies will share development costs and will co-commercialize it in the U.S., but Incyte will have exclusive rights outside the U.S.

- NEKTAR THERAPEUTICS' Kyvoda (oxycodegol, NKTR-181) – The FDA's Anesthetic and Analgesic Drug Products Advisory Committee, meeting jointly with the Drug Safety and Risk Management Advisory Committee, voted unanimously (27-0) ***against*** approval of this selective mu-agonist opioid to treat chronic low back pain. Nektar immediately withdrew its new drug application and terminated further development.

- NEOVASC's Reducer – The company submitted a pre-market approval (PMA) application for this device for treating refractory angina by increasing the perfusion of oxygenated blood to ischemic areas of the heart.

- Paclitaxel – A new meta-analysis of 8 trials with a total of 1,420 patients – by the same Greek interventional radiologist (Konstantinos Katsanos, MD, PhD) who did the first meta-analysis that raised questions about the safety of paclitaxel-coated/eluting peripheral artery disease (PAD) devices – looking at paclitaxel-coated balloons used to treat critical limb ischemia below-the-knee found the devices significantly *reduced* target lesion revascularization (TLR, a secondary endpoint, 11.8% vs. 25.6%) but significantly *increased* all-cause death and major amputation. The study was published in the ***Journal of Vascular Interventional Radiology***.

- PROTEUS DIGITAL HEALTH is giving up work on its digital pill technology for mental illness and cardiovascular health in the wake of the decision by Otsuka last month to end its deal on development of the technology.

- REFLOW MEDICAL's Temporary Spur Stent was granted breakthrough device status by the FDA for use in treatment of below-the-knee PAD.

- Robotic surgery – A study of the 169,404 patients undergoing surgery at 73 Michigan hospitals from 2012-2018, published in ***JAMA Network Open***, found that robot-assisted procedures in Michigan increased from 1.8% of all surgeries in 2012 to 15.1% in 2018.

- SGLT2 inhibitors – A 295,907-patient study, published in the ***Annals of Internal Medicine***, found that the incidence of gout was significantly lower in Type 2 diabetics taking an SGLT2 inhibitor vs. patients on a GLP-1 agonist.

- TAKEDA – ***Endpoints News*** reported that Takeda plans to spin off "a package of psych drugs," including therapies for schizophrenia and depression.

- TRANSENTERIX's Intelligent Surgical Unit, an add-on to the Senhance laparoscopic surgical system, was submitted to the FDA under the 510(k) pathway.

- Vaping update – In the latest numbers from the Centers for Disease Control and Prevention (CDC), 2,668 people have been hospitalized and 60 died from e-cigarette and vaping-associated lung injury (EVALI). The CDC also noted that

most EVALI patients (82%) reported having used a THC-containing product.

Very early research news

- Addiction – A mouse study by University of Minnesota Medical School researchers, published in ***Neuron***, suggests a possible new way to treat addiction – by targeting astrocyte calcium signaling. The researchers found that astrocytes respond to dopamine by increasing calcium in a brain reward center, and if astrocyte activity is restricted, the behavioral effects of amphetamine decrease.
- Obesity – Yale University researchers reported in ***Nature Communications*** on their discovery that an enzyme, O-GIcNAc transferase (OGT), plays a role in maintaining a healthy metabolism, suggesting that a drug targeting OGT might be used to treat obesity.
- Parkinson's disease – Scottish researchers reported in the journal ***Cell Reports*** that their roundworm studies suggest that a probiotic – *Bacilus subtilis* – can clear some of the alpha-synuclein clumps that are known to lead to the death of dopamine-producing nerve cells in the brain that causes tremors and movement difficulties in Parkinson's patients, suggesting a treatment targeting gut microbes might be a way to treat/prevent Parkinson's.

NEWS IN BRIEF

BRISTOL-MYERS SQUIBB

- CELGENE's Istodax (romidepsin). A mouse study by Yale University and Veterans Affairs researchers, published in ***Physiological Reports***, found that the hard-to-treat chronic pain that can result from second-degree burns may be the result of changes to neurons in multiple parts of the spinal cord, even far from the injury site. The researchers also found that a drug which blocks PAK1 – like the cancer drug romidepsin – might be repurposed to treat the long-lasting complications of second-degree burns.
- Sprycel (dasatinib). In a head-to-head trial, published in ***JAMA Oncology***, Sprycel significantly improved overall survival vs. Novartis' Gleevec (imatinib) in children with acute lymphoblastic leukemia (ALL) – 71.0% vs. 48.9% 4-year event-free survival and 88.4% vs. 69.2% overall survival.

CONCERTO HEALTHAI

- Is collaborating with **Johnson & Johnson/Janssen**, which will allow J&J to use its use-case engineered real-world data, enterprise artificial intelligence (AI) solutions, and scientific services.
- Expanded its collaboration with **Pfizer** on real-world data and artificial intelligence technologies in more disease areas.
- Is collaborating with **Texas Oncology/Precision Health Informatics** on real-world data solutions, research studies, and AI-enabled technologies.

Healthcare predictions

In an article in ***Health Affairs***, Premier CEO Susan DeVore made five predictions for 2020 healthcare:

1. More Medicare Advantage-style payment across federal reimbursement programs.
2. A significant reduction in drug shortages due to a combination of regulatory and market solutions.
3. More employers playing an even more active role in directly negotiating and contracting for better, more reliable services at a predictable cost for geographically diverse workforces.
4. New rules from the Office of the National Coordinator (ONC), mandating open application program interfaces that would enable a much more streamlined process for developing and bringing apps to the market.
5. The launch of a national demonstration of maternal bundles through the Center for Medicare and Medicaid Innovation.

LILLY

- Plans to offer two more generic insulin products at half-price in the U.S., new versions of Humalog Junior KwikPen and Humalog Mix75/25, with availability expected by mid-April.
- Ended its partnership with **NextCure**.

Multiple sclerosis (MS)

- An analysis of Medicaid data, published in ***Neurology***, found that spending on 15 MS drugs nearly tripled over 7 years, from $453 million in 2011 to $1.32 billion in 2017, driven primarily by increases in prescription costs which doubled during that period. The introduction of Novartis' Glatopa – a generic of Teva's Copaxone (glatiramer acetate) – had a "minimal effect."
- A survey by the National Multiple Sclerosis Society found that 40% of MS patients were changing how they take their disease-modifying therapies because of financial issues.

PFIZER

- Is collaborating with **Insilico Medicine** to use Insilico's artificial intelligence technology to help in drug discovery.

- **Reboxetine.** The U.S. rights to this investigational treatment for narcolepsy were licensed to **Axsome Therapeutics**.
- **Esreboxetine.** The exclusive U.S. rights to this investigational treatment for fibromyalgia were licensed to **Axsome Therapeutics**, which renamed it AXS-14.

ROCHE

- Signed a 15-year non-exclusive collaboration with **Illumina** to broaden patient access to genomic testing in oncology – combining Foundation Medicine's *in vitro* diagnostics with next-generation sequencing on Illumina's systems.
- **Risdiplam.** The company is offering a worldwide early access program for this spinal muscular atrophy therapy to Type 1 patients, with European patients able to get it immediately and in the U.S. when details are worked out with the FDA.
- **Rituxan (rituximab).** The 3.9-year, 989-patient SUNSTONE safety study of this anti-CD20 in rheumatoid arthritis by researchers at Oregon Health and Science University, published in ***Arthritis Care & Research***, found that the incidence of most adverse events were similar to those in historical data. However, the rates of clinically significant infections were higher than those in shorter trials or in registries (but lower than in a similar Medicare cohort).
- **Venclexta (venetoclax).** The company is collaborating with **Adaptive Biotechnologies** to use its clonoSEQ assay to assess minimal residual disease (MRD) in a Phase III trial of this anti-Bcl-2 in newly diagnosed chronic lymphocytic leukemia (CLL).

REGULATORY NEWS

Regulatory tidbits

- **Catheters.** The FDA issued draft guidance on 510(k) submissions for Class II peripheral percutaneous transluminal angioplasty balloon catheters and specialty catheters.
- **Genetic testing.** A law firm filed a citizen petition to the FDA on behalf of the Coalition to Preserve Access to Pharmacogenomics Information, urging the FDA to revise its previous safety communication to allow test makers and software companies to "communicate information about gene-drug interactions as part of genetic test reports." The petition also encourages the FDA to hold a public hearing.
- **Hospitals.** A federal judge denied a request by hospitals to enforce a ruling striking down the Center for Medicare and Medicaid Services' plan to institute site-neutral payments for doctor visits.
- **NDA to BLA.** The government spending bill means that some additional new drug applications (NDAs) to the FDA will become biologics license applications (BLAs) on March 23, 2020, because the bill amended the definition of "biological product" to remove the exception for chemically synthesized polypeptides.
  - **Ferring Pharmaceuticals' Acthrel** (corticorelin ovine triflutate) for Cushing's syndrome treatment.
  - **Pfizer's Elase-chloromycetin** (fibrinolysin and desoxyribonuclease combined, bovine, with chloramphenicol), a topical antimicrobial ointment.
  - **Sanofi's Adlyxin** (lixisenatide), a GLP-1 agonist for diabetes.
  - **Theratechnologies' Egrifta** (tesamorelin acetate) for excess stomach fat in HIV patients.
- **OND.** The FDA's reorganization of the Office of New Drugs (OND) was postponed but by just about a week, to January 21, 2020.
- **PMAs.** The FDA issued final guidance on annual reports required for approved premarket approval (PMA) applications.

Chinese coronavirus (now called 2019-nCoV)

- **WHO warning.** The World Health Organization (WHO) issued a warning to hospitals worldwide that this Chinese virus is no longer contained in China. WHO is considering convening an emergency meeting on the issue.
- **China health officials** reported that:
  - Most of the Chinese patients infected with 2019-nCoV, all in the city of Wuhan, had exposure to a large market where live animals were present, suggesting this is a novel virus that has jumped the species barrier to infect people.
  - Several hundred Chinese healthcare workers caring for outbreak patients are being monitored. No spread of the virus from patients to healthcare workers has been seen.
  - There is no ***sustained*** spread of this virus in the community, but there are indications that **some** limited person-to-person spread may have occurred.
  - In the latest numbers, 60 people have been infected with this coronavirus, with two deaths. Three cases have been reportd outside China, travelers from Wuhan – two in Thailand and one in Japan.
- **U.S. action.** In a teleconference with reporters, CDC officials announced that:
  - CDC and the Department of Homeland Security's Customs and Border Protection (CBP) were implementing

enhanced health screenings at three U.S. airports – Los Angeles (LAX), San Francisco (SFO), and New York Kennedy (JFK) – to detect ill travelers traveling to the United States on direct or connecting flights from Wuhan, China. The first flight to get the enhanced screening was a plane arriving at JFK directly from Wuhan at 10pm on January 17, 2020, with screenings at the other airports started the next day.

- Travelers will be questioned about symptoms (e.g., cough) and their temperature checked – much as was done during the Ebola outbreaks – and travelers suspected of possible 2019-nCoV infection will be transported to a so-far undisclosed New York facility for further tests, which initially will mean sending a specimen to the CDC and will likely take about a day to complete.
- About 5,000 travelers to the U.S. are expected to be screened over the next couple of weeks at those three U.S. airports. Currently, passengers leaving Wuhan's airport are ***not*** being screened, but China *may* begin exit screening. January is one of the two heaviest months for travel from China to the U.S.
- **The CDC expects there will be at least one case in the U.S.**
- CDC hopes to have a diagnostic test available for state public health labs soon, but for now all samples have to be tested at the CDC.
- The 2019-nCoV virus "looks like" the SARS and MERS coronaviruses, but that still needs more data.

FDA approvals/clearances

- AIDOC's artificial intelligence system for detection of large-vessel occlusions (LVOs) was granted 510(k) clearance.
- ALCON's Clareon, an intraocular lens (IOL) for cataract patients – both the standard and toric versions – was cleared for use with Alcon's AutonoMe pre-loaded delivery system.
- BIOCARDIA's Morph DNA, a deflectable guide catheter for use in navigating the Helix Biotherapeutic Delivery System during CardiAMP cell therapy delivery inside the heart, was granted 510(k) clearance.
- CUTTING EDGE SPINE's EVOL ha-DLIF, a direct lateral interbody fusion system, was granted 510(k) clearance in treating degenerative disc disease-related leg and back pain.
- LANNETT's Numbrino (cocaine hydrochloride nasal solution) was approved as a local anesthetic of mucous membranes during diagnostic procedures/surgeries in adult nasal cavities.
- NEURELIS' Valtoco (diazepam nasal spray) was approved for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity in epileptics age ≥6.
- NOVO NORDISK's Ozempic (injectable semaglutide) was granted a cardiovascular risk reduction indicator in adults with Type 2 diabetes and known cardiovascular disease.

FDA recalls/warnings

- BAYER's Essure – The FDA's Center for Devices and Radiological Health (CDRH) said Bayer has retrieved almost all of its unused Essure permanent birth control devices, with just 10 unused units still on the market. Bayer also completed enrollment in an FDA-mandated, 1,128-patient postmarketing study of the device.
- CARDINAL HEALTH's Level 3 surgical gowns and PreSource procedural packs – The FDA advised healthcare facilities to stop using these products due to potential quality and sterility issues.
- Duodenoscopes – The FDA issued a safety communication, urging transition to new devices with innovative designs that are easier to clean or are disposable.
- EISAI's Belviq (lorcaserin) – The FDA issued a warning that this obesity drug was associated in a clinical trial with a possible increase in cancer risk.
- FUSION IV PHARMACEUTICALS (dba AXIA Pharmaceutical) voluntarily recalled all unexpired, unused sterile drug products due to a lack of assurance of sterility.
- HEALTH PHARMA received a warning letter about violations of current good manufacturing practices (cGMP) at its New Jersey manufacturing facility, and the issues are serious enough that the FDA recommended the company hire a consultant to help with cGMP compliance.
- HUAIAN ZONGHENG BIO-TECH, a Chinese over-the-counter drug manufacturer, received a warning letter after the FDA discovered the company's plant in Huaian, China, sent drugs to the U.S. without testing the ingredients or retaining samples of the final products to see if they comply with specifications.
- Ranitidine – This week's recall due to NDMA contamination was by **Granules India**, which voluntarily recalled >23 million ranitidine pills from the U.S. market.
- PHILIPS' CombiDiagnost R90 GCF – The company issued an alert that this fluoroscopy system could be locked in a "Table Up/Down" state when that tilting feature is used, which could result in the entry of a contrast agent into the brain and pose the risk of headache. In addition, the thermo switch on the system's power distribution unit might not

function correctly, and that could cause the device to overheat.

European Regulatory News

- *Germany*. BAYER's Vitrakvi (larotrectinib) – The Institute for Quality and Efficiency in Health Care (IQWiG) said this treatment for NTRK fusion-positive tumors has not been proven to provide an added benefit. In particular, IQWiG had a problem with the lack of a comparator arm in the trials.
- *U.K. - Scotland* – ROCHE's Ocrevus (ocrelizumab) was approved by the Scottish Medicines Consortium (SMC) as a treatment for early, inflammatory primary progressive multiple sclerosis (PPMS) patients with symptoms <15 years and active inflammation on MRI.
- ISO. The European Medicines Agency (EMA) will make the ISO's individual case safety report format mandatory when reporting suspected adverse reactions to EudraVigilance, effective June 30, 2022.
- ABBVIE's merger with Allergan will require divestiture of Allergan's brazikumab, an anti-IL-23.
- BIOLINERX's motixafortide (BL-8040) was granted orphan drug status by the European Commission as a treatment for pancreatic cancer.
- EMERGENT BIOSOLUTIONS' CHIKV VLP – The EMA told the company it could start a Phase III trial of this chikungunya vaccine.
- HEMOVENT's MOBYBOX Runner, an extracorporeal life support system for treating patients in cardiac arrest or profound circulatory shock, was granted a CE Mark.
- LEO PHARMA's Picato (ingenol mebutate) – The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) recommend use of this gel for treating actinic keratosis be stopped while it reviews the drug's safety. The concern is a possible link between Picato and development of skin cancer.
- MEDTRONIC's InterStim Micro – a rechargeable sacral neurostimulation device for overactive bladder, fecal incontinence, and non-obstructive urinary retention – and InterStim SureScan MRI leads were both granted a CE Mark.
- STAAR SURGICAL's Evo/Evo+ and Visian implantable collamer lenses were all granted a CE Mark for use as supplemental lenses in patients undergoing cataract surgery.
- SILVER BULLET THERAPEUTICS' OrthoFuzIon, a bone screw system with an AntiBacterIon coating for use in orthopedic reduction and internal fixation, was granted a CE Mark.

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

- ASTELLAS' Xospata (gilteritinib) – NICE rejected this FLT-3 inhibitor for relapsed/refractory FLT3+ acute myeloid leukemia (AML) because of uncertainty about the long-term survival benefit – and because of price.
- ASTRAZENECA's Lynparza (olaparib) – NICE recommended use of this PAPR inhibitor in adults with relapsed, platinum-sensitive BRCA1/2 mutated ovarian, fallopian tube, or peritoneal cancer.
- BAYER's Vitrakvi (larotrectinib) – NICE rejected this tumor-agnostic cancer drug over cost-effectiveness, rejecting the company's proposed discount.
- MERCK's Keytruda (pembrolizumab) – NICE rejected use of this PD-1 inhibitor for untreated metastatic/unresectable recurrent head and neck squamous cell carcinoma (HNSCC) over a lack of evidence in people whose cancer started outside the mouth – and, of course, because of cost-effectiveness.
- NOVARTIS' inclisiran – Novartis is collaborating with the National Health Service (NHS) on a large primary prevention trial of this siRNA treatment for hypercholesterolemia. Novartis and the NHS also are partnering to make the drug widely available once it has both EMA and NICE approval.
- PFIZER's Ibrance (palbociclib) – NICE recommended use of this CDK4/6 inhibitor to treat HR+, HER2-negative advanced breast cancer in patients who already had endocrine therapy.

Regulatory news from other countries

- *Australia*. Inhalers – Therapeutic Goods Administration said that during the bushfires pharmacies can advertise puffers and other salbutamol inhalers even though advertising of the devices is normally banned.
- *China*.
  - Regulations – The National Medical Products Administration, the European Medicines Agency, the European Commission's DG Sante, and others are collaborating on identification of similarities/differences between their regulatory systems for active pharmaceutical ingredients.
  - VICTREX/VICTREX HONG KONG and Yingkow Xingfu Chemical formed a joint venture to build and operate a new PEEK polymer manufacturing facility in Liaoning, China.

- ***Japan.*** ROIVANT SCIENCES/DERMAVANT SCIENCES' tapinarof – Exclusive rights in Japan to this topical AhR agonist for psoriasis and atopic dermatitis were licensed to **Japan Tobacco/Torii Pharmaceutical**.

- ***South Korea.*** The Ministry of Food and Drug Safety and **Swissmedic** agreed to mutual recognition of each other's good manufacturing practice inspection results for medicinal products and agreed to exchange other documents, information, and inspection reports.

2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
January tba	**Aimmune Therapeutics' Palforzia** (AR-101) to treat peanut allergy	PDUFA date (*estimated to be in mid-January*)
January 23	**Epizyme's tazemetostat** for metastatic/locally-advanced epithelioid sarcoma	PDUFA date
January 24	**Merck MSD's Dificid** (fidaxomicin) for *Clostridium difficile* infections	PDUFA date
February 4	Testing methods for **asbestos in talc** and cosmetic products containing talc	FDA public meeting
February 5	Oncology Center of Excellence – **product development for 2025**	FDA public workshop
February 14	**Blueprint Medicines' Ayvakit** (avapritinib, BLU-285) for ***fourth-line*** GIST	PDUFA date
February 16	**Agile Therapeutics' Twirla** (AG200-15, 120 μg levonorgestrel + 30 μg ethinyl estradiol), a contraceptive patch	PDUFA date *Extended by the FDA from November 16, 2019*
February 18	**Merck MSD's Keytruda** (pembrolizumab) – 6 sBLAs for a 30-minute Q6W infusion to treat melanoma, Hodgkin's lymphoma, primary mediastinal large B-cell lymphoma, gastric cancer, hepatocellular carcinoma, and Merkel cell carcinoma	PDUFA date
February 19	**Adverse event reporting** using ICH standards	FDA public meeting
February 21	**Alder BioPharmaceuticals' eptinezumab** (ALD-403), a CGRP inhibitor for migraine	PDUFA date
February 21	**Esperion Therapeutics' bempedoic acid** monotherapy to treat hypercholesterolemia	PDUFA date
February 24	**FDA Rare Disease Day:** Supporting the future of rare disease product development	FDA public meeting
Feb. 25-26	Discussion of the evolving role of **artificial intelligence in radiological imaging**	FDA public workshop
February 26	**Acacia Pharma's Barhemsys** (IV amisulpride) for post-operative nausea and vomiting (PONV)	PDUFA date
February 26	**Esperion Therapeutics' bempedoic acid in combination with ezetimibe** to treat hypercholesterolemia	PDUFA date
February 27	**BeiGene's zanubrutinib**, a BTK inhibitor for mantle cell lymphoma	PDUFA date
March 3	Development of **individualized therapeutics**	FDA workshop
March 4	Selection of strains for the 2020/2021 flu vaccine	FDA's Vaccines and Related Biological Products Advisory Committee
March 5	Advancing animal models for antibacterial drug development	FDA public workshop
March 5	Medical extended reality: evaluation practices for virtual and augmented reality	FDA public workshop
March 8	**Horizon Therapeutics' teprotumumab** to treat active thyroid eye disease	PDUFA date
March 9	**Intarcia Therapeutics' ITCA-650** (exenatide implant) for Type 2 diabetes	PDUFA date
March 10	**Bristol-Myers Squibb's Opdivo** (nivolumab) **+ Yervoy** (ipilimumab) for advanced hepatocellular carcinoma	PDUFA date
March 10	Patient-focused drug development for **stimulant use disorder**	FDA public meeting
March 15	**Astellas and Seattle Genetics' enfortumab vendotin**, an antibody-drug conjugate for treating metastatic/locally-advanced urothelial cancer	PDUFA date
March 17	**Eton Pharmaceuticals' ET-105** (reformulated lamotrigine) as adjunctive therapy for partial seizures in Lennox-Gastaut syndrome patients	PDUFA date
March 23	Identification of concepts and terminology for **multi-component biomarkers**	FDA workshop
March 25	**Bristol-Myers Squibb/Celgene's ozanimod** (RPC-1063) for relapsing multiple sclerosis	PDUFA date
March 25	**Zogenix's Fintepla** (fenfluramine, ZX-008) for Dravet syndrome	PDUFA date
March 26	**Heron Therapeutics' HTX-011** (bupivacaine + meloxicam) for postoperative pain	PDUFA date
March 26	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	PDUFA date ***postponed until June 26***
March 26	**IntelGenx Technologies' Rizaport** (RHB-103) for migraine	PDUFA date
March 27	**Modernizing FDA's data strategy**	FDA public meeting
March 28	**Rockwell Medical's Triferic** (ferric pyrophosphate) for anemia	PDUFA date
March tba	**AstraZeneca's Imfinzi** (durvalumab) + tremelimumab for small cell lung cancer	PDUFA date (*estimated late March*)

more - 2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
April tba	**Lilly's empagliflozin + linagliptin + metformin extended-release**, a triplet for Type 2 diabetes	PDUFA date
April tba	**Puma Biotechnology's Nerlynx** (neratinib) – expanded approval as a ≥3-line treatment for HER2+ metastatic breast cancer	PDUFA date
April 4	**Bristol-Myers Squibb/Celgene and Acceleron Pharma's Reblozyl** (luspatercept-aamt) – expanded approval to include very low to intermediate risk myelodysplastic syndrome-associated anemia in patients with ring sideroblasts who require red blood cell transfusions	PDUFA date
April 22 *tentative*	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	FDA's Gastrointestinal Drugs Advisory Committee
April 25	**Sanofi's MenQuadfi**, a meningococcal vaccine	PDUFA date
April 26	**Neurocrine Biosciences' opicapone** to treat Parkinson's disease	PDUFA date
April 27	**United Therapeutics' Trevyent** (treprostinil) to treat pulmonary arterial hypertension (PAH)	PDUFA date
April 30	**Sanofi's isatuximab** for relapsed/refractory multiple myeloma	PDUFA date
May 4	**2020 generic drug** regulatory science initiatives	FDA public workshop
May 12	**Johnson & Johnson and Halozyme's Darzalex** (daratumumab) subcutaneous delivery for multiple myeloma	PDUFA date (*estimated*)
May 12-13	**Regulatory education for industry**	FDA conference
May 14	**Sunovion Pharmaceuticals' dasotraline** for moderate-to-severe binge eating disorders	PDUFA date
May 15	**Allergan's bimatoprost sustained-release** for treating glaucoma	PDUFA date (*estimated*)
May 15	**Clovis Oncology's Rubraca** (rucaparib) – expanded approval to treat advanced prostate cancer	PDUFA date
May 24	**Roche's risdiplam** (RG-7916) to treat spinal muscular atrophy	PDUFA date
May 25	**Evofem Biosciences' Amphora** (L-lactic acid + citric acid + potassium bitartrate), a hormone-free contraceptive (resubmission)	PDUFA date
May 30	**Incyte's pemigatinib** for previously treated, locally-advanced/metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements	PDUFA date
June 2	**Immunomedics' sacituzumab govitecan** (IMMU-132) as a ≥3-line treatment for metastatic triple-negative breast cancer	PDUFA date
June 2	**Foamix Pharmaceuticals' FMX-103** (minocycline foam) to treat moderate-to-severe papulopustular rosacea	PDUFA date
June 11	**Viela Bio's inebilizumab** for first-line monotherapy of neuromyelitis optica spectrum disorder	PDUFA date
June 26	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	PDUFA date ***extended from March 26***
July 13	**Averitas Pharma's Qutenza** (capsaicin patch) – expanded approval to treat neuropathic pain from diabetic peripheral neuropathy	PDUFA date
August 5	**DBV Technologies' Viaskin Peanut** for treating children with peanut allergy	FDA target action date
August 27	**Cassiopea's clascoterone cream 1%**, a topical androgen receptor inhibitor for acne	PDUFA date
Sept. 28-30	Global summit on regulatory science: **Emerging Techologies**	FDA summit **https://aralliance.org/gsrs/**
October 24	**Spectrum Pharmaceuticals' Rolontis** (eflapegrastim) for treating chemotherapy-induced neutropenia	PDUFA date