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

- ✓ Coronavirus (Covid-19) has slowed in China but is spreading rapidly in other parts of the world, particularly Italy, South Korea, and now the U.S., where 22 people have died. (*See Page 3 for the key developments.*)
- ✓ Ebola – The outbreak in the Democratic Republic of the Congo appears finally to be under control.
- ✓ GILEAD SCIENCES is buying Forty Seven for $4.9 billion.
- ✓ INSULET's Omnipod Horizon – A software glitch caused a halt to a pivotal trial of this insulin pump.
- ✓ THERMO FISHER SCIENTIFIC is buying Qiagen for $11.5 billion.
- ✓ **Positive trial news:**
  - KARYOPHARM THERAPEUTICS' Xpovio (selinexor) in a Phase III in multiple myeloma.
  - MERCK MSD's Keytruda (pembrolizumab) beat Seattle Genetics' Adcetris (brentuximab vedotin) in a confirmatory Phase III trial in relapsed/refractory classical Hodgkin's lymphoma.
- ✓ **Negative trial news:**
  - ABBVIE and ROCHE's Venclexta (venetoclax) in the required postmarketing confirmatory trial in AML.
  - ASTRAZENECA's Imfinzi (durvalumab) in a postmarketing confirmatory trial in inoperable bladder cancer.

SHORT TAKES

- AKREVIA THERAPEUTICS changed its name to Xilio Therapeutics.
- AMGEN's Prolia (denosumab) – A 508-patient study, published in the journal ***Bone***, found that this RANKL inhibitor increased bone mineral density (BMD). Denosumab also lowered the incidence of new vertebral fractures in postmenopausal women with diabetes and osteoporosis vs. placebo (1.6% vs. 8.0%). However, denosumab was associated with a greater incidence of new non-vertebral fractures (most often the forearm and rib) in women with diabetes but not in women without diabetes.
- ARSENAL CAPITAL PARTNERS bought BresMed Health Solutions, which provides health economic research, communications, and consulting services.
- ASTRAZENECA's Imfinzi (durvalumab) – This PD-L1 inhibitor, in combination with tremelimumab (a CTLA4 inhibitor), missed the primary endpoint in the postmarketing

confirmatory DANUBE trial in inoperable bladder cancer, failing to prolong overall survival vs. chemotherapy. Adding to the bad news, Imfinzi alone failed to prolong survival vs. chemotherapy, which could endanger its accelerated approval in this indication.

- Breast cancer – A study by Fox Chase Cancer Center researchers, published in ***Cancer Medicine***, found that neo-adjuvant chemotherapy does not expedite the start or completion of breast cancer treatment vs. performing surgery first.

- BRISTOL-MYERS SQUIBB is collaborating with **Voluntis** on development of a digital cancer companion app for cancer patients on its therapies.

- CAREDX's AlloSure – Data from 11 transplant centers, published in the ***American Journal of Transplantation***, showed this dd-cfDNA test can identify patients with T-cell mediated rejection (TCMR) 1A and borderline allograft rejection who are at elevated risk of graft injury.

- DIASORIN exclusively licensed **TTP**'s Puckdx platform for use in human *in vitro* diagnostic assays.

- Ebola update – The World Health Organization (WHO) said there hasn't been a new case of Ebola in the Democratic Republic of the Congo in two weeks, and the last positive patient was released from treatment, which suggests the outbreak there may now be over.

- EXACT SCIENCES bought **Paradigm Diagnostics** and **Viomics**, which expands its ability to do oncology testing and research.

- GILEAD SCIENCES is buying **Forty Seven** for $4.9 billion.

- GLAXOSMITHKLINE reportedly is looking for a buyer for some of its antibiotics.

- Influenza – The Centers for Disease Control and Prevention (CDC) said the flu vaccine has been 50% effective this year against influenza B/Victoria viruses and 37% effective against influenza A (H1N1).

- INSULET's Omnipod Horizon – Due to a software glitch in the Personal Diabetes Manager (PDM) software with the Omnipod Dash insulin management system for this insulin pump, Insulet said it is pausing a pivotal trial.

- INTEGRITY IMPLANTS' FlareHawk – A retrospective study of this expandable cage for spinal surgery showed a positive fusion rate, with 96.6% of patients achieving fusion.

- JOHNSON & JOHNSON/JANSSEN's ponesimod, an S1P1 modulator, was submitted to the European Medicines Agency (EMA) as a treatment for adults with relapsing multiple sclerosis (MS).

- KARYOPHARM THERAPEUTICS' Xpovio (selinexor), a once-weekly oral SINE inhibitor, met the primary endpoint in the Phase III BOSTON trial – in combination with once-weekly Takeda's Velcade (bortezomib) + low-dose dexamethasone – vs. twice-weekly Vel/dex alone in multiple myeloma patients, significantly increasing progression-free survival (PFS) – 13.93 months vs. 9.46 months (p=0.0066).

- KURA ONCOLOGY's tipifarnib was granted fast track status by the FDA as a treatment for adults with relapsed/refractory angioimmunoblastic T-cell lymphoma, nodal peripheral T-cell lymphoma with T follicular helper phenotype, and follicular T-cell lymphoma.

- LILLY's Trulicity (dulaglutide) lowered HbA_{1c} significantly better than Novo Nordisk's Victoza (liraglutide) in a real-world, head-to-head study in Type 2 diabetics, published in the journal ***Metabolism***. Compared to AstraZeneca's Byetta (exenatide), there was no significant difference in HbA_{1c} lowering.

- MORPHOSYS and INCYTE's tafasitamab (MOR-208) – The companies announced that they got antitrust clearance for their collaboration and license agreement on this off-the-shelf CAR T treatment, in combination with lenalidomide, for relapsed/refractory diffuse large B-cell lymphoma (DLBCL), which is under review by the FDA, with an August 30, 2020, PDUFA date.

- NEURONETICS' NeuroStar, a transcranial magnetic stimulation (TMS) device, was granted breakthrough device status by the FDA as a treatment for bipolar depression.

- NEVRO sued **Nalu Medical**, which is developing a minimally invasive spinal cord stimulator, for patent infringement.

- PFIZER and LILLY's tanezumab – The FDA accepted for review a biologics license application (BLA) for this subcutaneous anti-NGF drug to treat moderate-to-severe osteoarthritis pain. The PDUFA date is in December 2020. An advisory committee review is expected.

- PIVOTAL, a Spanish contract research organization (CRO), bought **Akcelis**, a clinical trial specialist.

- PLURISTEM THERAPEUTICS' PLX-R18 – U.S. Biomedical Advanced Research and Development Authority (BARDA) ***rejected*** the company's request for funding to conduct a study to compare this placenta-derived allogeneic cell therapy to standard of care in treating acute radiation syndrome (ARS).

- **Psychedelics** – A rat study, published in the journal ***Chemical Neuroscience***, compared ketamine, psilocybin, and lysergic acid diethylamide (LSD) head-to-head and found that the psychedelics (psilocybin and LSD) had a longer-acting antidepressant effect than ketamine.

- **SHIONOGI** expanded its collaboration with **Tetra Therapeutics** and got an option to buy the company, which would give it BPN-14770, a PDE-4D inhibitor for Alzheimer's disease, Fragile X syndrome, and other brain disorders.

- **SUMITOMO DAINIPPON PHARMA/UROVANT SCIENCES' vibegron** – The FDA accepted for review a new drug application (NDA) for this small molecule beta-3 agonist (bought from Merck) as a treatment for overactive bladder. The PDUFA date is December 26, 2020.

- **THERMO FISHER SCIENTIFIC** is buying **Qiagen** for $11.5 billion.

- **TREVENA's Olinvo (oliceridine)**, an IV mu-opioid receptor agonist, was resubmitted to the FDA as a treatment for moderate-to-severe pain in hospitalized patients. *Remember, the FDA rejected it in 2018, issuing a complete response letter.* The new PDUFA date is August 7, 2020.

- **XATEK's ClotChip**, an investigational portable blood-clotting sensor, was granted breakthrough device status by the FDA.

NEWS IN BRIEF

ABBVIE

- **and ROCHE's Venclexta (venetoclax)** missed the primary endpoint in the confirmatory trial required by the FDA as part of its accelerated approval, failing to significantly prolong overall survival when added to low-dose chemotherapy (with cytarabine) vs. chemotherapy alone in patients with acute myeloid leukemia (AML) – 7.2 months vs. 4.1 months, p=0.11. *This endangers its FDA approval.*

- The acquisition of **Allergan** got clearance from the European Commission but still needs the blessing of the U.S. Federal Trade Commission.

MERCK MSD

- **Keytruda (pembrolizumab).** In interim data this PD-1 inhibitor beat Seattle Genetics' Adcetris (brentuximab vedotin), an antibody-drug conjugate, in the head-to-head, confirmatory Phase III KEYNOTE-204 trial in relapsed/refractory classical Hodgkin's lymphoma, showing significantly longer progression-free survival.

- **Ervebo.** The CDC's Advisory Committee on Immunization Practices (ACIP) recommended use of this Ebola Zaire vaccine for adults at high risk for the disease.

NOVARTIS

- **Beovu (brolucizumab-dbll).** Novartis defended the safety profile of this anti-VEGF treatment for wet age-related macular degeneration (AMD), saying the side effects that have been reported by the American Society of Retina Specialists (ASRS) and to the FDA's FAERS database are within the labeled rate. ASRS had reports of 14 cases of retinal vasculitis, 11 of which were occlusive retinal vasculitis.

- **LXE-408.** Novartis is partnering with India's Drugs for Neglected Diseases initiative (DNDi) on development of this investigational treatment for kala azar (visceral leishmaniasis). Novartis will handle Phase I trials and global distribution at "an affordable basis." DNDi will lead Phase II and III trials.

- Is collaborating with **Orionis Biosciences** on discovery and design of small molecule therapeutics, such as protein degraders, using Orionis' Allo-Glue technology platform.

ROCHE/GENENTECH

- **Elecsys GALAD score**, an algorithmic score for aiding in the diagnosis of hepatocellular carcinoma, was granted breakthrough device status by the FDA.

- **Esbriet (pirfenidone)** was granted breakthrough therapy designation by the FDA as a treatment for unclassifiable interstitial lung disease (uILD).

- **Tominersen (RG-6042, formerly IONIS-HTT-Rx).** A small Phase I trial of this antisense drug, licensed from Ionis Pharmaceuticals, was halted due to serious side effects in two patients – both intrathecal catheter-related infections considered not-related to the study drug.

CORONAVIRUS UPDATE

There is a lot of coronavirus news this week, so this is an expanded section.

- **Extent of the problem.**
  - Worldwide >109,000 people have been diagnosed with Covid-19, the virus has affected people in 104 countries, and >3,800 people have died.
  - Italy is particularly hard hit, with >7,300 cases and ≥366 deaths. One-fourth of the country (16 million people) is in a lockdown similar to that imposed in China, though whether Italians will comply as well remains to be seen.

- Community spread of Covid-19 is now occurring in the U.S. Excluding people who were repatriated from China or from cruise ships, the U.S. has >500 people diagnosed with the virus across at least 34 states, and 22 people have died. Thousands of Americans (including >10,000 in California alone) are in quarantine or home isolation.
- Carnival's Grand Princess, off the coast of California, has an outbreak of the virus. CDC flew test kits to the ship, and of the 46 people tested, 21 (19 crew and 2 passengers) were positive. The ship is headed to Oakland CA to unload passengers. California residents will be quarantined on a military base in California, and the other passengers will go either to a military base in Texas or Georgia. The crew will remain on the ship.
- A cruise ship on the Nile River in Egypt has been quarantined after ≥45 passengers tested positive.
- The WHO's latest estimate is that the fatality rate is 3.4%, back where it appeared to be in the early days of the outbreak in China. So, even if the fatality rate were only 2.4% for Covid-19, that is 24 times the rate for flu (<0.1%).

The virus. There are reports that the SARS-CoV-2 virus has mutated into a second strain, similar to the first but different. Chinese researchers have described it as an older, milder "S" version that has been circulating for some time and a newer, more aggressive and dangerous "L" version.

Resources.

- Congress voted **$8.3 billion** to fight the coronavirus. This includes >$3 billion for vaccine research.
- **Premier** said that 54% of hospitals responding to its member survey have initiated personal protection equipment (PPE) conservation protocols to stretch their supplies. Premier said it is working with suppliers, distributors, members, CDC, and the FDA to ensure access to supplies in the event of a surge in demand. Premier will hold a congressional briefing on March 12 focused on actions Congress can take to help front-line caregivers respond to coronavirus and other public health emergencies.

Diagnostics. Is the CDC test finally reliable? That isn't an unreasonable question. And there are other tests available. The newest are:

- **AES Venture's The Reader**, a device that uses a lateral flow immunoassay (developed by researchers in the United Arab Emirates), that reportedly can detect different viruses in blood, including SARS-CoV-2, with results in 10 minutes. The accuracy was described as similar to a pregnancy test.
- **BGI's Real-Time Fluorescent RT-PCR kit**, which uses bronchoalveolar lavage fluid and throat swab samples, was granted a CE-IVD Mark by the EMA.
- **ELITech Group and OsangHealthcare's GeneFinder Covid-19 Plus RealAmp kit** for detecting SARS-CoV-2 was given a CE Mark.
- **LabCorp and Quest** – Each lab launched its own Covid-19 test for use and will apply to the FDA for an emergency use authorization (EUA).
- **Snibe Diagnostic's Maglumi 2019-nCoV** (SARS-CoV-2) IgM/IgG kits, which are already in use in Chinese hospitals, were granted a CE Mark and are heading to hospitals in Italy.
- **Home testing** will become available soon in the Seattle area, courtesy of the Bill and Melinda Gates Foundation. The foundation will offer home-testing kits that allow people who are concerned they are infected to swab their nose and send the sample back for analysis, with results expected in 1-2 days. Initially, their lab expects to be able to handle 400 tests/day, increasing to thousands/day.

Treatment.

- The U.S. government reportedly is considering using disaster relief funds to pay hospitals to treat *uninsured* Covid-19 patients.
- **Alnylam Pharmaceuticals** is collaborating with **Vir Biotechnology** and claims to be "relatively close" to identification of an RNAi candidate for treating Covid-19.
- **Gilead Sciences' remdesivir** – There are now at least 5 trials underway or about to get underway with the drug – two in China, one by the National Institute of Allergy and Infectious Diseases (NIAID) being run by the University of Nebraska, and two in the U.S. run by Gilead.
- **NanoViricides** is the latest company to announce it is working on a treatment, in this case a broad-spectrum virus-binding ligand.
- **Roche's Actemra (tocilizumab)** was added to Covid-19 treatment guidelines in China. It makes sense since this anti-IL-6 is used to treat the respiratory reaction that immunotherapy patients sometimes get, cytokine release syndrome (CRS).
- **Takeda's TAK-888**, a plasma-derived therapy made from the blood of Covid-19 patients who have recovered, is under development.

■ **Vaccines.** Anthony Fauci, MD, PhD, director of the NIAID, said "For now, the answer I,s not going to be a vaccine. If we go into a cycle where we come back next year, then we will have some opportunity for a vaccine."

- The latest potential SARS-CoV-2 vaccine in development is by **Migal Research Institute** in Israel, which had been developing a coronavirus vaccine for chickens and is now modifying it for humans. Human trials are expected to start in a few months.
- **Pfizer** told ***Reuters*** that it is considering working with **BioNTech** on an mRNA vaccine.

■ **Business interruptions.**

- Numerous companies have ordered their workers to work from home. **Biogen** ordered most employees to work from home after five cases were linked to a Biogen meeting in a Boston hotel. **Lilly** also asked workers to work from home.
- More than a few major medical centers and drug and biotech companies have restricted employee travel.
- **Stanford University** canceled all campus classes for the semester, having students complete classes online. Other major universities are looking at doing the same thing.
- **Siemens Healthineers** announced that it is pulling out of ***all*** trade shows for the month of March due to concerns over the spread of the coronavirus.
- The **cruise industry** can't be in good shape. If the three cruise ship horror stories – Diamond Princess, Grand Princess, and ship in Egypt – haven't scared customers away, the U.S. State Department now is advising Americans to avoid traveling on cruise ships. And NIAID's Dr. Fauci said simply, "Absolutely don't get on a cruise ship."

■ **Drug supply chain.** **India** restricted exports of 26 active pharmaceutical ingredients (APIs), including paracetamol, progesterone, and some antibiotics (e.g., tinidazole).

■ **Summer and Covid-19.** While it is possible that the coronavirus will die out with summer, there are several reasons that may not happen, including:

- It is summer in Brazil, but they are having an outbreak there.
- It is a novel virus, so there is no natural community immunity.
- This is a different virus, so it isn't known yet whether it is temperature sensitive.
- Even if it does fade, it is likely to come back. At this point, it does not look like a one-time scare, like Zika. And Covid-19 also could turn out to be a 2-year cycle virus, like acute flaccid myelitis.

■ **Medical conference impact.** At least 7 major medical conferences in March were canceled, all on short notice due to coronavirus, with another 5 postponed. Six meetings are still trying to hold on, but that may change when word spreads that ***someone at the ACTRIMS meeting in West Palm Beach in late February was Covid-19 positive***. There are no details on gender, name, condition except that the person did visit the Biogen booth.

- ***Canceled*** – The **Acute Cardiovascular Care 2020** conference, scheduled for March 7-9 in Athens. It is uncertain whether it will be rescheduled. The European Society of Cardiology said its other scheduled conferences this year are still going ahead as planned – at least for now.
- ***Changed to virtual only*** – **Conference on Retroviruses and Opportunistic Infections** (CROI) in Boston, March 8-11.
- ***Canceled*** – The **Healthcare Information and Management Systems Society** (HIMSS) meeting – the premier health and information technology meeting – scheduled to start March 9 in Orlando.
- ***Postponed*** – The **European Congress of Radiology** (ECR), scheduled for March 11-15 in Vienna, Austria, has been postponed to July 15-19, 2020.
- ***Canceled*** – **American Academy of Allergy, Asthma, and Immunology (AAAAI)**, which was scheduled for March 13-16 in Philadelphia.
- ***Postponed*** – The **European Breast Cancer Conference** (EBCC12) scheduled for March 18-20 in Barcelona, Spain, was rescheduled for September 30-October 2.
- ***Canceled*** – America's Health Insurance Plans' (AHIP) **National Health Policy Conference**, scheduled for March 18-20 in Washington, DC.
- ***Canceled*** – **American Society for Clinical Pharmacology and Therapeutics** (ASCPT) meeting in Houston, March 18-21.
- ***Postponed*** – The **National Comprehensive Cancer Network** (NCCN) postponed its annual conference, scheduled for March 19-22 in Orlando, citing "precautions against potential patient exposure to Covid-19." A new date has not yet been announced.
- ***Canceled*** – The **American College of Healthcare Executives** (ACHE), scheduled for March 23-26 in Chicago. It will ***not*** be rescheduled.
- ***Postponed*** – The **International Papillomavirus Conference** (IPVC) meeting scheduled for March 23-27 in Barcelona, Spain. No new date is available yet.

- ***Postponed*** – **Society of Surgical Oncology 2020 International Conference on Surgical Cancer Care** scheduled for March 25-28 in Boston was postponed until August 17-20.
- ***Canceled*** – The **American Board of Radiology** (ABR) canceled the Diagnostic Radiology (DR) Certifying Exam and the Radioisotope Safety Exam (RISE) tests scheduled for April 6 in Tucson, AZ.
- ***Meetings of particular interest that are still scheduled in March, but keep your plans flexible:***
  - ✓ Renal Physicians Association, March 19-22, Baltimore.
  - ✓ American Academy of Dermatology (AAD), March 20-24 in Denver.
  - ✓ American Academy of Orthopedic Surgeons (AAOS), March 24-28 in Orlando.
  - ✓ American College of Cardiology (ACC), March 28-30 in Chicago.
  - ✓ ENDO 2020, March 28-31 in San Francisco.
  - ✓ Gene Therapy for Rare Disorders, March 30-April 2 in Boston.

■ **Unanswered questions.** The questions that are ***still*** unanswered about Covid-19 and the coronavirus (SARS-CoV-2) include:

- *Does the coronavirus persist in a non-human host during the off-season?*
- With respect to pets:
  - ✓ *Can a cat or dog or other pet become infected with coronavirus?*
  - ✓ *Can a cat or dog or other pet transmit the virus* either if infected or simply by carrying it in its mouth or on its fur?
- *Is SARS-CoV-2 more like measles or more like flu?* Will a SARS-CoV-2 vaccine continue to be effective year-after-year like measles, or will a new formulation be necessary each season as with the flu?
- *Does a person develop immunity after surviving a coronavirus infection* or can a person get Covid-19 more than once?
- *Is there a reservoir in the body where the virus can hide as with HIV or Ebola,* and later come out to affect the carrier or to infect other people?
- *Is the transmission rate affected by the level of infection?* That is, can mildly infected people transmit the virus as easily or as much as heavily infected people? Can you get the virus as easily from an asymptomatic infected person as from a symptomatic infected person?
- *Why is "isolation at home" considered an acceptable approach for an infected person without symptoms?* Are there any penalties if a person leaves his/her home and exposes others?
- *How long does SARS-CoV-2 live on surfaces?* We know how long other coronaviruses can live on different surfaces. The ***New York Times*** cited a study which found that they can live 2 hours on steel and copper and up to 9 days on plastic and cardboard.
- *How are doctors outside of China treating the hospitalized patients with confirmed Covid-19?* Are they using an anti-IL-6 (Roche's Actemra, tocilizumab)? If not tocilizumab, what treatments are patients getting outside of the clinical trials of Gilead Sciences' remdesivir? U.S. doctors who have treated Covid-19 patients with severe disease have been unusually quiet about what they tried.

REGULATORY NEWS

Regulatory tidbits

■ **Artificial intelligence.** The FDA finalized rules for artificial intelligence-based image acquisition and optimization software. It will initially apply to ultrasound imaging technology, but it could be expanded to other imaging applications and modalities in the future.

■ **Bone anchors.** The FDA issued final guidance for 510(k) submissions for bone anchors.

■ **Diagnostics.** The Verifying Accurate, Leading-edge IVCT Development (VALID) Act, which would give the FDA authority to review and approve *in vitro* clinical tests (e.g. laboratory-made assays and test kits) was introduced with bipartisan support. The bill also would create a new category for these tests.

■ **Drug imports.**

- New Mexico passed a law that will allow the state to seek FDA approval to import cheaper drugs from Canada.
- A bill was introduced in the U.S. Senate by Sen. Martha McSally (R-AZ) that would lower prescription drug prices by letting Medicare negotiate prices for off-patent drugs. The legislation also would allow Americans to purchase drugs from Canada in some circumstances.

■ **Medical devices.** FDA Commissioner Stephen Hahn, MD, called on Congress to release new reporting requirements mandating that medical device manufacturers notify the FDA about the possibility of any supply-chain disruptions or medical device shortages – as pharmas are required to do about drug shortages.

- Metformin. The FDA did not find unacceptable contamination with NDMA in this diabetes drug, but a citizen petition filed with the FDA by an outside laboratory, **Valisure**, disputes that finding. Valisure found high levels of NDMA in 42% of the batches of metformin it tested.

FDA approvals/clearances

- ACCESS VASCULAR's HydroPICC, a peripherally-inserted central catheter, was cleared for use.
- ALCON's Vivity, a trifocal presbyopia-correcting intraocular lens (PC-IOL), was cleared for use in both standard and toric versions for cataract patients.
- ALLERGAN's Durysta (biodegradable bimatoprost implant) was approved to reduce intraocular pressure (IOP) in patients with glaucoma or ocular hypertension.
- CEROVENE's pyrimethamine, the first generic version of Turing Pharmaceuticals' Daraprim, was approved to treat toxoplasmosis.
- Face masks – The FDA approved the CDC's request to allow respirators approved by the National Institute for Occupational Safety and Health (NIOSH) to be used by healthcare professionals (not the general public) during the coronavirus outbreak.
- LIFE SPINE's Lateral ProLift Expandable System, an expandable cage for spine surgery, was granted expanded 510(k) clearance.
- MAGNOLIA MEDICAL TECHNOLOGIES' Steripath Gen2, a specimen diversion device line for use in reducing blood contamination or for infusion after sample collection, was granted 510(k) clearance.
- MEDI-TATE's iTind, a transurethrally inserted device for treating benign prostatic hyperplasia, was granted de novo clearance.
- NOVARTIS' Isturisa (osilodrostat) was approved to treat adults with Cushing's disease.
- PENUMBRA's Jet 7x, an aspiration catheter for stroke thrombectomy, was cleared for use.
- SANOFI's Sarclisa (isatuximab-irfc), an anti-CD38, was approved for use, in combination with Bristol-Myers Squibb/Celgene's Pomalyst (pomalidomide) and dexamethasone, as a third-line treatment for multiple myeloma.
- UPNRIDE ROBOTICS' UPnRIDE, a *standing* robotic wheelchair, was cleared for use.

FDA recalls/warnings

- ACINO PRODUCTS received a warning letter after an FDA inspection of its over-the-counter suppository manufacturing facility in New Jersey found missing testing documentation and "filthy" equipment held together with tape and plastic wrap.
- ADVANCED BIONICS' HiRes Ultra and Ultra 3D cochlear implants were voluntarily recalled due to hearing degradation complaints.
- BECTON DICKINSON/CAREFUSION 303's Alaris System Infusion Pumps were recalled (Class I) due to software and system errors.
- Cannabidiol (CBD) – The FDA issued a warning that the "myriad of CBD products" on the market have not been evaluated by the FDA and determined to be safe. The Agency is concerned that people may think using CBD "can't hurt."
- CIPLA received a warning letter about contamination at its manufacturing plant in Goa, India.
- Cybersecurity – The FDA warned healthcare providers and medical device manufacturers about a group of 12 cybersecurity risks – called SweynTooth – that hackers could use to gain access to device functions and cause problems with pacemakers, glucose monitors, etc. The risks are related to Bluetooth Low Energy wireless communication technology.
- Electroshock behavior-control devices – electrical stimulation devices, sometimes used to treat self-harm and aggression in people with intellectual or developmental disabilities – were banned.
- HIKMA PHARMACEUTICALS' ketorolac tromethamine injection – A voluntary recall was expanded, and production halted, after visible black, oily particulate was observed.
- INTEGRA LIFESCIENCES' NeuraGen Nerve Guides – A voluntary recall and field safety notice was issued after one lot of parts was found out of specification in a finished goods release test.
- MEDTRONIC's Pipeline Flex embolization devices were recalled – and a field safety notice issued – due to the potential for fracture at the distal section.
- MERCK MSD's Singulair and generic montelukast – The FDA strengthened the warning about the risk of neuropsychiatric events with this asthma and allergy medication.
- OUTLOOK PHARMACEUTICALS' ProCentra (dextroamphetamine sulfate) – The company received a warning letter for failing to include any risk information in a sponsored link on Google for this treatment for attention-deficit/hyperactivity disorder (ADHD). The company was also cited for misbranding because the drug's generic name was not included.

European Regulatory News

- ABBVIE's Maviret (glecaprevir + pibrentasvir, Mavyret in the U.S.) – The European Commission approved this 8-week treatment for treatment-naïve hepatitis C virus (HCV) patients with genotype 3 and compensated cirrhosis.
- CRYOLIFE's On-X, an ascending aortic prosthesis used to treat diseased, damaged, or malfunctioning prosthetic and native heart valves in the aortic position involving an ascending aortic aneurysm, received a CE Mark.
- DXTERITY DIAGNOSTICS' DxCollect MicroCollection Tube, a fingerstick blood collection device that can stabilize DNA and RNA for 2 weeks at room temperature, was granted a CE Mark.
- GLAXOSMITHKLINE and INNOVIVA's Trelegy Ellipta (fluticasone furoate + umeclidinium + vilanterol inhalation powder) – The EMA accepted a marketing application for review that seeks expanded use to treat asthma.
- RANDOX LABORATORIES' STI assay, a multiplex test for sexually transmitted infections (STIs), was granted a CE Mark.
- V-WAVE's Ventura, a minimally-invasive interatrial shunt system for patients with heart failure, was granted a CE Mark.

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

- BRISTOL-MYERS SQUIBB/CELGENE's Revlimid (lenalidomide) – NICE recommended use with Roche's MabThera (rituximab, Rituxan in the U.S.) to treat adults with previously treated follicular lymphoma (Grade 1-3A).

2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
March 9	**Intarcia Therapeutics' ITCA-650** (exenatide implant) for Type 2 diabetes	PDUFA date
March 9	Competitive marketplace for **biosimilars**	FDA/FTC public workshop
March 9	Detection of **circulating tumor DNA** for cancer screening	FDA public workshop
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 11	Use of **over-the-counter antiseptics** in the food handler setting	FDA's Non-Prescription Drugs Advisory Committee
March 12	U.S.-Japan **cellular and gene therapy conference**: Exosomes in cancer treatments and other diseases	FDA conference in conjunction with Japan's Ministry of Education, Culture, Sports, Science, and Technology
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' EM-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 MS	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 *Extended by the FDA to June 26, 2020*
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 30	Patient-focused drug development for **vitiligo**	FDA public meeting
March 31	Use of patient preference information **in medical device regulatory decisions** – risk:benefit and beyond	FDA public workshop
March tba	**AstraZeneca's Imfinzi** (durvalumab) + tremelimumab for small cell lung cancer	PDUFA date (*estimated late March*)
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 1	FDA communications about the **safety of medical devices**	FDA public meeting
April 2	Reducing the risk of **Zika virus transmission** in blood and blood components	FDA's Blood Products Advisory Committee
April 3	Testing for **hepatitis B** surface antigen (HBsAg) in blood donations	FDA's Blood Products Advisory Committee
April 3	Consultation on **International Council for Harmonisation** (ICH)	FDA and Health Canada joint meeting
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 6	**America's Got Regulatory Science Talent Winners**	FDA presentation
April 7	**Medical device user fee amendments** for fiscal years 2023-2027	FDA public meeting
April 13-15	Good **simulation practices** in health technologies	FDA public workshop
April 14	Preparations for international cooperation on **cosmetics regulation**	FDA public meeting
April 20-21	Annual **Sentinel** review	FDA public workshop
April 21	**GlaxoSmithKline's Trelegy Ellipta** (fluticasone furoate + umeclidinium + vilanterol inhalation powder) – claim for reduction in all-cause mortality in COPD	FDA's Pulmonary-Allergy Drugs Advisory Committee
April 22 *tentative*	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	FDA's Gastrointestinal Drugs Advisory Committee *This is not on the FDA calendar, but the company gave the date*
April 23	**Lilly/Avid Radiopharmaceuticals' flortaucipir F18**, an IV radioactive diagnostic agent for PET imaging of the brain	FDA's Medical Imaging Drugs Advisory Committee
April 23	Reclassification of **facet screws** from unclassified to Class II	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee
April 24	**Classification to Class II of three devices** that are currently unclassified: semicon-strained toe joint prostheses; intracompartmental pressure monitors; and intra-abdominal pressure monitoring devices	FDA's Orthopaedic and Rehabilitation Devices Advisory Committee

more - 2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
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 29	Topic not announced yet	FDA's Pediatric Advisory Committee
April 30	**Sanofi's isatuximab** for relapsed/refractory multiple myeloma	PDUFA date
May 4	**2020 generic drug** regulatory science initiatives	FDA public workshop
May 8	Development of **antifungal drugs to treat Valley Fever** (coccidioidomycosis)	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 14	**Blueprint Medicines' Ayvakit** (avapritinib, BLU-285) for *fourth-line* GIST	PDUFA date *extended by FDA from February 14*
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 15	**DBV Technologies' Viaskin Peanut** for treating children with peanut allergy	FDA's Allergenic Products Advisory Committee
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 26	**Regeneron Pharmaceuticals and Sanofi's Dupixent** (dupilumab) – expanded approval to include treatment of children age 6-11 with atopic dermatitis	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 4	**Merck MSD's Recarbrio** (imipenem + cilastatin + relebactam) – expanded approval to treat hospital-acquired Gram-negative bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP)	PDUFA date
June 11	**Viela Bio's inebilizumab** for first-line monotherapy of neuromyelitis optica spectrum disorder	PDUFA date
June 18	**Epizyme's Tazverik** (tazemetostat) – expanded approval to treat relapsed/ refractory follicular lymphoma	PDUFA date
June 19	**Roche's Tecentriq** (atezolizumab) – expanded use as first-line treatment for advanced NSCLC with high PD-L1 expression and no ALK or EGFR mutations	PDUFA date
June 26	**Heron Therapeutics' HTX-011** (bupivacaine + meloxicam) for postoperative pain	PDUFA date *Extended by the FDA from March 26*
June 26	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	PDUFA date *extended from March 26*
June 27-July 1	**AFDO annual educational conference**	FDA's National Center for Toxicological Research
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 7	**Trevena's Olinvo** (oliceridine) for moderate-to-severe pain in hospitalized patients	PDUFA date
August 10	**Gilead Sciences/Kite Pharma's KTE-X19** for relapsed/refractory mantle cell lymphoma	PDUFA date
August 13	**Deciphera Pharmaceuticals' ripretinib** (DCC-2618) for GIST	PDUFA date
August 17	**Bristol-Myers Squibb/Celgene/Juno Therapeutics' lisocabtagene maraleucel** (JCAR-017, liso-cel) for DLBCL	PDUFA date
August 20	**Seattle Genetics' tucatinib** – in combination with Roche's Herceptin + Xeloda – to treat breast cancer	PDUFA date
August 21	**BioMarin Pharmaceutical's valoctocogene roxaparvovec**, a gene therapy for hemophilia A	PDUFA date

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Date	**Topic**	**Committee/Event**
August 27	**Cassiopea's clascoterone cream 1%**, a topical androgen receptor inhibitor for acne	PDUFA date
August 30	**MorphoSys and Incyte's tafasitamab** for use in combination with lenalidomide to treat relapsed/refractory diffuse large B-cell lymphoma	PDUFA date
September 27	**Aquestive Therapeutics' Libervant** (diazepam buccal film) for seizure clusters in epileptics	PDUFA date
Sept. 28-30	Global summit on regulatory science: **Emerging Techologies**	FDA summit **https://aralliance.org/gsrs/**
October 18	**Roche's Herceptin** (trastuzumab) **+ Perjeta** (pertuzumab) – a fixed dose combination to treat HER2+ breast cancer	PDUFA date
October 24	**Spectrum Pharmaceuticals' Rolontis** (eflapegrastim) for treating chemotherapy-induced neutropenia	PDUFA date
November 15	**Alkermes' ALKS-3831** (olanzapine + samidorphan) for bipolar I disorder and schizophrenia	PDUFA date
November 25	**Revance Therapeutics' daxibotulinumtoxinA** for moderate-to-severe glabellar lines	PDUFA date
December tba	**Pfizer and Lilly's tanezumab** to treat moderate-to-severe osteoarthritis pain	PDUFA date
December 3	**BioCryst Pharmaceuticals' berotralstat** (BCX-7353) for hereditary angioedema attacks	PDUFA date
December 20	**FibroGen and AstraZeneca's roxadustat** for anemia of chronic kidney disease	PDUFA date
December 26	**Sumitomo Dainippon Pharma/Urovant Sciences' vibegron** for overactive bladder	PDUFA date