TRENDS-in-MEDICINE

November 22, 2020

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: The Covid-19 news that occurred after our Coronavirus Update on November 18 is included here, starting on Page 3, and there was more than you might expect in just 4 days. Have a **Happy Thanksgiving!**

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

- ✓ **ADAMIS PHARMACEUTICALS and US WORLDMEDS' ZIMHI** (APC-6000, naloxone injection) – The FDA rejected this opioid overdose treatment for the second time.
- ✓ **ALKERMES' ALKS-3831** (olanzapine + samidorphan) was rejected by the FDA to treat bipolar I disorder and schizophrenia.
- ✓ **BOSTON SCIENTIFIC's Lotus Edge**, a TAVR, was discontinued and withdrawn from the market.
- ✓ **CELLECTIS' UCARTCS1** – The FDA lifted the clinical hold on a Phase I trial of this off-the-shelf T cell therapy in relapsed/refractory multiple myeloma.
- ✓ **PFIZER and BIONTECH's BNT162b2** was the first Covid-19 vaccine to be submitted to the FDA for an EUA, and the FDA set a December 10 date for an advisory committee review.
- ✓ **Positive trial news:**
  - **CELLDEX THERAPEUTICS' CDX-1401** – in melanoma.
  - **GILEAD SCIENCES' lenacapavir** – in multi-class drug resistant HIV.
  - **PTC THERAPEUTICS' Translarna** (ataluren) – for symptoms of AADC-d and for nonsense mutation Duchenne muscular dystrophy.
  - **SUMITOMO/UROVANT SCIENCES' vibegron** – in overactive bladder.
  - **UNIQURE and CSL BEHRING's etranacogene dezaparvovec** – a gene therapy for hemophilia B.
- ✓ **Negative trial news:** **BRAINSTORM CELL THERAPEUTICS' NurOwn** – stem cell therapy for amyotrophic lateral sclerosis (ALS).

SHORT TAKES

- **ABCELLERA** bought **Trianni**, which gives it a line of genetically-engineered mice for generating panels of human antibodies with drug-like properties.

- **ADAMIS PHARMACEUTICALS and US WORLDMEDS' ZIMHI (APC-6000, naloxone injection)** – For the second time the FDA rejected this new formulation of naloxone for treating opioid overdoses, issuing a complete response letter that cited issues with chemistry, manufacturing, and controls (CMC). *Remember, the FDA also rejected this drug in November 2019 over different CMC issues.*

- **ADC THERAPEUTICS' loncastuximab tesirine (Lonca, ADCT-402)** – The FDA accepted for review and granted priority review to this antibody-drug conjugate for relapsed/refractory diffuse large B-cell lymphoma (DLBCL). The PDUFA date is May 21, 2021.

- **ALKERMES' ALKS-3831 (olanzapine + samidorphan)** was rejected by the FDA as a treatment for bipolar I disorder and schizophrenia. The FDA issued a complete response letter, citing issues with the tablet coating process. Alkermes believes that issue is resolved. *Remember, last month an FDA advisory committee recommended approval.*

- **AMYLYX PHARMACEUTICALS' AMX-0035 (sodium phenylbutyrate + tauroursodeoxycholic acid)** was granted orphan drug status by the FDA as a treatment for Wolfram syndrome, a rare neurological disease.

- **APELLIS PHARMACEUTICALS' pegcetacoplan** – The FDA accepted the new drug application (NDA) for this complement C3 inhibitor to treat paroxysmal nocturnal hemoglobinuria (PNH) and granted it priority review. An advisory committee review is not expected. The PDUFA date is May 14, 2021.

- **ARCHIGEN BIOTECH**, a joint venture that Samsung Biologics and AstraZeneca created to develop SAIT-101, a biosimilar of Roche's Rituxan (rituximab), for follicular lymphoma is being dissolved, and development of SAIT-101 is being abandoned.

- **BEIGENE's tislelizumab** – This PD-L1 inhibitor met the primary endpoint in the 805-patient Phase III RATIONALE-303 trial in PD-L1+ metastatic ≥2-line non-small cell lung cancer (NSCLC), significantly prolonging overall survival vs. docetaxel.

- **BIOMARIN PHARMACEUTICAL** is collaborating with **Deep Genomics** to use artificial intelligence in drug discovery.

- **BIONTECH's BNT-113** – The company is partnering with **Qiagen** on development of a tissue-based companion diagnostic that can identify HPV+ squamous cell carcinoma of the head and neck for this anti-CD40 mRNA cancer vaccine.

- **BOSTON SCIENTIFIC's Lotus Edge**, a transcatheter aortic valve replacement (TAVR), was discontinued – and all the unused devices in the market are being recalled – due to issues with the delivery system.

- **BRAINSTORM CELL THERAPEUTICS' NurOwn**, a stem cell therapy for amyotrophic lateral sclerosis (ALS), missed the primary endpoint in an ~50-patient Phase III trial, failing to significantly beat placebo on response rate (35% vs. 28%). The company blamed the failure on a higher-than-expected placebo response and hopes to convince the FDA to review it anyway. And that might be possible since a pre-specified analysis of patients with early ALS showed a bigger improvement in response rate with NurOwn (35% vs. 16%), and NurOwn patients had a smaller decline on a functional scale (-1.77 vs. -3.78).

- **BRISTOL-MYERS SQUIBB/CELGENE/JUNO THERAPEUTICS' lisocabtagene maraleucel (JCAR-017, liso-cel)** – The FDA once again delayed a decision on this CAR T therapy for diffuse large B-cell lymphoma (DLBCL), saying it could not complete the inspection of the Houston manufacturing facility before the November 16, 2020, PDUFA date. No new PDUFA date has been set.

- **CELLDEX THERAPEUTICS' CDX-1401** – A 60-patient Phase II study, published in ***Nature Cancer***, found this dendritic-cell targeting melanoma cancer vaccine was nearly twice as effective at Month 4 when patients were also given a Flt3L + Oncovir's poly-ICLC.

- **CELLECTIS' UCARTCS1** – The FDA lifted the clinical hold on the Phase I MELANI-01 trial of this off-the-shelf T cell therapy in relapsed/refractory multiple myeloma that was imposed after a patient died. The trial protocol was modified to enhance patient safety.

- **GE HEALTHCARE** bought **Prismatic Sensors** which makes CT imaging detectors.

- **GILEAD SCIENCES' lenacapavir** – This long-acting capsid inhibitor met the primary endpoint in the 36-patient Phase II/III CAPELLA trial in HIV-1 patients with multi-class drug resistance and a detectable viral load on a failing regimen, with significantly more lenacapavir patients achieving ≥0.5 $\log_{10}$ reduction in viral load at Day 14 vs. placebo (88% vs. 17%).

- **LILLY** is partnering with **Precision BioSciences** on genome editing, using Precision's ARCUS genome editing platform and focusing on Duchenne muscular dystrophy and two other undisclosed targets.

- **LUPIN PHARMACEUTICALS' Solosec (secnidazole)** – The FDA accepted for review a supplemental new drug application (sNDA) for expanded approval of this broad spectrum antibiotic to treat trichomoniasis in adults and adolescents. The PDUFA date is June 30, 2021.

- **MESOBLAST's remestemcel-L** – The global rights to this mesenchymal stem cell treatment for acute respiratory distress syndrome (ARDS) were licensed to **Novartis**, including use to treat Covid-19 if that pans out.

- **PTC THERAPEUTICS' Translarna (ataluren)** – Data presented at the virtual ISPOR Europe conference showed that symptoms of aromatic L-amino acid decarboxylase deficiency (AADC-d) contribute to a high disease burden, and another study in nonsense mutation Duchenne muscular dystrophy, caregivers reported positive changes in their child's condition with Translarna. Both studies reinforce the importance of treating these patients early.

- **RETROPHIN** changed its name to **Travere Therapeutics**.

- **ROCHE** is collaborating with **Lead Pharma** on oral small molecules to treat immune-mediated diseases.

- **SANOFI's avalglucosidase alfa** – The FDA accepted a biologics license application (BLA) for this next-generation enzyme replacement therapy as a long-term treatment for Pompe disease and granted it priority review. The PDUFA date is May 18, 2021.

- **SUMITOMO/UROVANT SCIENCES' vibegron** – The results of the 52-week EMPOWUR extension trial of this beta-3 agonist, presented at the International Continence Society virtual meeting, showed long-term improvements in quality-of-life markers (coping, sleep, and social interaction) as well as incontinence in adults with overactive bladder.

- **SYNTHETICMR's SyMRI MSK**, a software solution that provides MRI sequences that could help diagnose musculoskeletal issues, was submitted to the FDA through the 510(k) pathway.

- **UNIQURE and CSL BEHRING's etranacogene dezaparvovec** – This second-generation gene therapy met the primary endpoint in the 54-patient HOPE-B trial in adults with moderate-to-severe hemophilia B, eliminating bleeding events through Month 6 in 39 patients. All but 2 patients discontinued routine preventive treatment.

- **VIIV HEALTHCARE's cabotegravir**, an integrase inhibitor, was granted breakthrough therapy designation by the FDA as a pre-exposure prophylaxis (PrEP) in HIV.

- **VIVET THERAPEUTICS and PFIZER's VTX-801** – The FDA gave a green light for the Phase I/II GATEWAY trial of this r-AAV-based gene therapy vector to treat Wilson disease, and the trial is expected to start in early 2021.

Animal health news

- **ABCELLERA** expanded its antibody discovery collaboration with **Invetx** on therapeutics for *animals*.

- **QBIOTICS GROUP's Stelfonta (tigilanol tiglate injection)** was approved by the FDA to treat *dogs* with non-metastatic cutaneous mast cell tumors. This is the first approval for an intratumoral injection to treat this cancer in dogs.

- **ZOETIS' Librela (bedinvetmab)** was approved by the European Commission as a monthly treatment for the pain of osteoarthritis in *dogs*.

Very early research news

- **Over-drinking** – Canadian researchers reported in ***Scientific Reports*** that they have developed a device that uses hyperventilation to help eliminate excess alcohol from people who have had too much to drink.

COVID-19 UPDATE

- **The numbers**
  - ***Worldwide.*** There have been 58,395,671 cases with 1,384,651 deaths (a case fatality rate of 2.4% and a per capita rate of 18 per 100,000).
  - ***U.S.*** There have been 12,126,076 cases with 256,163 deaths (a case fatality rate of 2.1% and a per capita rate of 78 per 100,000). That is up from 76 per 100,000 just 4 days ago, but all of the countries with highest per capita fatality rates 4 days ago have increased as well.
- **Europe**
  - The European Commission approved Austria's plan (the Fixkostenzuschuss Phase II scheme) to pick up the uncovered fixed costs of businesses affected by the coronavirus pandemic.
  - The World Health Organization (WHO) is predicting a "tough" six months ahead for Europe.

U.S.

- **Travel.** The Centers for Disease Control and Prevention (CDC) urged Americans not to travel for the Thanksgiving holiday, to stay home and limit the holiday to household members, not outside guests. They didn't mention the Christmas holidays, which are likely to be even harder to control than Thanksgiving travel.

- **Parties.** Florida Gulf Coast University in Fort Myers – Students caught partying in groups >10 run the risk of being expelled – and then banned from attending ***any*** public college or university in the state for a full year. And some students found out that the threat is real.

- **Curfews.** Experts in the U.S. are also warning of a tough winter. As a result of the ongoing surge in cases and hospitalizations:

  ✓ California officials imposed a statewide **curfew** for 41 counties, restricting non-essential work and gatherings from 10pm to 5am. During the overnight lockdown period, people will still be allowed to go to the grocery store or the drug store, walk the dog, or pick up restaurant takeout food.

  ✓ In New York, Massachusetts, and Iowa the governor ordered bars (even ones that serve food) and restaurants to close at 10pm.

  ✓ Miami-Dade, Florida, continues to have a 12M-6am curfew.

  ✓ Ohio has a 10pm-5am curfew.

- **Health system views.** Officials from two major health systems held press briefings this week to talk about Covid-19.

  ✓ **Cleveland Clinic** – which will have vaccine distribution sites in both Florida and Ohio:

  - ***Case increases.*** Robert Wyllie, MD, chief medical operations officer, said the number of cases per day in Ohio increased from 1,380 on April 19 to 1,733 on July 28, to 7,787 on November 19 (with 14.2% of everyone tested showing positive for Covid-19). The recent increase was blamed on kids going back to school, cooler weather driving people indoors, and "pandemic fatigue." He said Covid-19 currently is taking up twice as many beds as the flu, adding that it is easier to control the flu than Covid-19.

  - ***Vaccines.*** Serpil Erzurum, MD, a pulmonologist and the chief research and academic officer, predicted that the Covid-19 vaccines will "change how we make vaccines for our lifetime. These are proof of the concept that the RNA vaccine approach works." Asked how long the vaccine is protective, she said that isn't known yet, adding, "I imagine it will vary from person to person." She said that for the country to return to "normal" 40%-70% of the country needs to be vaccinated.

  - ***Transmission.*** Steven Gordon, MD, chairman of the Department of Infectious Disease, said it was initially thought that you had a 20% chance of getting Covid-19 if someone in the household had the virus, but new data suggest 53% of household contacts get Covid-19.

  - ***Treatment.*** Dr. Gordon said Lilly's bamlanivimab, an antibody cocktail, is "not a game-changing product. The clinical benefits are clearly modest. It requires outpatient treatments in Covid-19-positive patients, which is a challenge."

  - ***Testing.*** Dr. Gordon called Lucira Health's home Covid-19 test "an ice-breaker in many ways. It is not as great as RT-PCR, but it is certainly better than the antigen test. This is for people with symptoms, not asymptomatic people. This can be a big game changer in the future – like pumping your own gas." He said the Cleveland Clinic has never offered antibody testing, "At the individual level it is not informative. At the population level it is. At the individual level, I would advise you to use your money [on something else]."

  - ***Holidays.*** Dr. Gordon said the restrictions being urged for Thanksgiving are going to continue through Christmas.

  - ***Healthcare workers.*** Dr. Wyllie said that 500 Cleveland Clinic workers in Ohio and 50 in Florida have Covid-19 and cautioned that if the number goes above 900, healthcare delivery for other conditions will have to be restricted and staff reassigned from other departments to Covid-19.

  ✓ **Henry Ford Health System** – Adnan Munkarah, MD, executive vice president/chief clinical officer, said one-third of people with *symptoms* suggestive of Covid-19 are testing positive for the virus.

  - ***Healthcare workers.*** Over the past 8 months, 10,600 employees have been tested for Covid-19, and >1,600 have tested positive. Over the past 7 days, 169 healthcare workers tested positive, "so staffing is a significant concern for us…If we cannot stop the community spread, maintaining healthcare is not going to be sustainable…This is a public health issue."

- ***Christmas.*** Dr. Munkarah said, "I wish I could say that by Christmas everything will be okay and everyone can be together…but whatever holidays people are celebrating over the next couple of months, we need to be very careful and use the same measures and precautions."
- ***Vaccine distribution.*** Asked about guidelines recommending healthcare workers be vaccinated ahead of the elderly, who are at much greater risk of death from Covid-19, Dr. Munkarah said there probably won't even be enough vaccine doses for healthcare workers in the first phase, but he expects "some" high-risk patients to get vaccinated in the *second* part of Phase I – if there is enough vaccine – adding, "There are reasons people feel the need for them to be out there because of the risk of exposure …but I'm not sure there is a right or wrong answer."

■ **Testing. Oxford Immunotec Global's T-SPOT Discovery SARS-CoV-2 test kit –** A cohort study of ~3,000 essential workers (e.g., police, fire, and healthcare workers) in the U.K., published online at ***medRxiv***, found that this molecular PCR test detected confirmed SARS-CoV-2 infection that was not positive in antibody testing. None of the participants with a high T-cell response developed Covid-19 in the follow-up period, but those with a low T-cell response were at risk of developing Covid-19. The study suggests that antibody testing alone is not enough and may underestimate the working-age population who are at lower risk of Covid-19. The researchers also noted that high levels of SARS-CoV-2 responsive T cells decline with age, which may explain higher illness incidence and severity in older people.

■ **Treatments**

- **Gilead Science's Veklury (remdesivir) –** A WHO panel recommended ***against*** use of this antiviral to treat hospitalized Covid-19 patients, saying there is "no evidence" that it improves survival or shortens recovery time. The recommendation was published in ***The BMJ***.
- **Lilly and Incyte's Olumiant (baricitinib)**, an oral JAK inhibitor approved to treat arthritis, was granted an emergency use authorization (EUA) for use in combination with Gilead Sciences' Veklury (remdesivir) to treat hospitalized Covid-19 patients age ≥2 on oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- **Lilly's bamlanivimab –** The Infectious Diseases Society of America (IDSA) quickly revised its guidelines to include a recommendation ***against*** the routine use of this antibody cocktail in ambulatory patients with Covid-19 but stated that, for patients at increased risk, "bamlanivimab is a reasonable treatment option if, after informed decision-making, the patient puts a high value on the uncertain benefits and a low value on uncertain adverse events."
- **Regeneron Pharmaceuticals' REGN-COV2 (casirivimab + imdevimab) –** This antibody cocktail treatment for mild-to-moderate Covid-19 patients at high risk of progressing to severe Covid-19 – the treatment President Trump received – was granted an EUA by the FDA.
- **Roche's Actemra (tocilizumab) –** In the early days of the pandemic, this anti-IL-6 looked promising as a treatment for the cytokine release syndrome associated with Covid-19, but all the trials were negative. However, REMAP-CAP, a global trial network that has been testing different Covid-19 drugs in an adaptive fashion at 200 sites in 19 countries, announced that Actemra worked in their study. The data safety and monitoring board reviewed data from 303 patients and determined that Actemra had a 99.75% chance of being better for the sickest Covid-19 patients than giving them no immune modulator at all. Just how much Actemra helped is still not clear.

■ **Vaccines**

- **AstraZeneca and the University of Oxford's AZD-1222 (ChAdOx1nCoV-19) –** The results with the 560 patients in the Phase II portion of a Phase II/III trial, published in ***The Lancet***, showed that this Covid-19 vaccine produced similar immune responses in people age >70 as in people age 56-69 or 18-55. The data also suggest the vaccine is ***better tolerated*** by seniors than younger people.
- **Inovio Pharmaceuticals' INO-4800 –** The FDA lifted the partial clinical hold on this investigational Covid-19 vaccine and said the company can proceed with the Phase II portion of the planned Phase II/III INNOVATE trial. The Phase III portion remains on partial clinical hold until issues with the delivery device are resolved.
- **Moderna's mRNA-1273 –** The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) started a rolling review of this Covid-19 vaccine.
- **Pfizer and BioNTech's BNT162b2** was submitted to the FDA for an EUA, and Moderna's mRNA-1273 is expected to be submitted in the next few days. Peter Marks, MD, PhD, director of the FDA's Center for Biologics Evaluation and Research (CBER) said the reviews are likely to take weeks, not days. The FDA's Vaccines and Related Biological Products Advisory Committee is scheduled to review Pfizer and BioNTech's vaccine on December 10, 2020. The FDA intends to live stream the VRBPAC meeting on the Agency's YouTube, Facebook,

and Twitter channels; the meeting will also be webcast from the FDA website.

- **Distribution** – The White House Coronavirus Task Force said that the government is ready to start shipping vaccine doses to pharmacies and other distribution sites within 24 hours of the FDA granting an EUA. *But are pharmacies really ready for this?* A check with our local CVS in small town Jensen Beach FL, was surprising: They are ready to go. They have a freezer, they have planned for pharmacists giving the shots, and they have applied to get technicians approved to give the shots to expand their capability. Their only real questions are: When are we getting the vaccine? How much will we get? They do expect more demand than supply to start. It is possible, and perhaps even likely, that vaccinations will be restricted to residents, so you may not be able to travel to another state to get vaccinated.

- **Who will get the vaccine first?**

  ✓ **U.S.** – Adm. Brett Giroir, MD, Assistant Sec. for Health at the Department of Health and Human Services (HHS) and the Trump administration testing czar, confirmed the plan the CDC's Advisory Committee on Immunization Practices (ACIP) endorsed in October – healthcare workers first, followed by the elderly.

  ✓ **U.K.** – The U.K. vaccination schedule is different from that proposed for the U.S. The U.K. will vaccinate people in care homes first, then people age ≥80, then people age ≥75. Where healthcare workers should be prioritized in the U.K. will depend "on the characteristics of the vaccines when they become available and the epidemiology of disease at the time of delivery."

- **Vaccine attitudes**

  ✓ ***Survey #1*** – This survey, conducted by OnePoll and commissioned by DocASAP (a patient access platform), asked 1,000 U.S. adults who had visited a doctor in the last 12 months where they would feel safe getting the Covid-19 vaccine:

  ~50% doctor's office (up from 25% in July 2020).

  33% a hospital.

  29% a pharmacy.

  16% a grocery store with a walk-in clinic.

  15% a retail store with a walk-in clinic.

  7% drive-through vaccination site.

  ✓ ***Survey #2*** – A Gallup survey of 2,985 adults in late October found that 58% were willing to get a Covid-19 vaccine (up from 50% in September but down from 66% in June). The most common reason for hesitation was concern over the rushed development.

REGULATORY NEWS

Regulatory tidbits

- **Biosimilars** – The FDA issued draft guidance in question-and-answer format on development and licensure of biosimilar and interchangeable biological products.

- **Doc talks** – The HHS' Office of Inspector General (OIG) issued a "Special Fraud Alert," telling pharmas and medical device companies that paid healthcare provider speaker programs – at company sponsored events – which have been on hold because of Covid-19, should ***not*** resume after the pandemic.

- **Drug prices** – President Trump finalized two measures designed to lower drug prices. Both still have to withstand pharma/device company legal challenges as well as Biden administration potential changes.

  - "Most favored nations" approach – matching the lowest price among a group of other developed countries – for what Medicare pays for drugs administered in a doctor's office.

  - Require rebates for brand drugs to go to Medicare beneficiaries, not insurers or pharmacy benefit managers.

- **Emergency use authorizations (EUAs)** – The FDA's Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) announced additional steps to increase transparency in their review of data supporting EUAs, saying the Agency wants to be "as transparent as possible under the law" about the scientific basis for an EUA recommendation by releasing all the information they can legally release.

- **Oncology drugs** – The FDA issued draft guidance on cross-labeling of oncology drugs. The FDA said that, traditionally, sponsors have not requested cross-labeling – changes to the labeling of a previously approved drug that describes how to use that drug in a new regimen – but recently there has been an increase in applications proposing cross-labeling for oncology drug combination regimens. This is FDA's attempt to start a discussion on how this should be done.

- **Oral contraceptives** – The FDA issued draft guidance on interaction studies with combined oral contraceptives.

- **Orphan drugs** – The U.S. House of Representatives unanimously passed a bill (H.R. 4712) that would require drug companies to prove they don't expect to recover research and development costs through U.S. sales over 12 years in order to obtain 7-year marketing exclusivity as an orphan drug. The legislation closes a loophole.

- **Product-specific guidances** – The FDA issued 34 (13 new and 21 revised) product-specific guidances for products used to treat diseases/conditions such as attention-deficient/hyperactivity disorder, ulcerative colitis, and hypertension as well as complex devices such as a metered dose inhaler with epinephrine (Amphastar Pharmaceuticals' Primatene Mist) or Boehringer Ingelheim's Spiriva Respimat (tiotropium bromide).
- **Robotics** – The CDC gave a grant for $1.5 million over 3 years to the University of Illinois at Chicago and Worcester Polytechnic Institute to research ways to reduce exposure to workplace hazards using robotics, focusing on healthcare and manufacturing.

FDA approvals/clearances

- **ALLOTROPE MEDICAL's StimSite**, a device that helps surgeons identify and locate ureters using electrical stimulation, was cleared for use.
- **ARMIS BIOPHARMA's VeriFixx**, a small bone implant for the fixation of osteotomies and reconstruction of the lesser toes following correction procedures for hammertoe, claw toe, and mallet toe, was cleared for use.
- **EIGER BIOPHARMACEUTICALS' Zokinvy (lonafarnib)** was approved to treat Hutchinson-Gilford progeria syndrome and some progeroid laminopathies.
- **LANTHEUS'** artificial intelligence-enabled bone scan index solution for prostate cancer was granted 510(k) clearance for use with GE Healthcare's Xeleris platform.
- **SAFKAN HEALTH's OtoSet**, an ear-cleaning system for removing impacted earwax, was granted 510(k) clearance.

FDA recalls/warnings

- **Covid-19** – The FDA and the Federal Trade Commission (FTC) jointly sent a warning letter to **Pro Breath MD** (dba Dentist Select and OraCare) for selling unapproved products with fraudulent Covid-19 claims.
- **FRESENIUS KABI's dexmedetomidine** – One lot was recalled due to contamination with lidocaine.

European Regulatory News

- **ALEXION PHARMACEUTICALS' Ultomiris (ravulizumab)** was approved by the European Commission to treat paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS).
- **ALNYLAM PHARMACEUTICALS' Oxlumo (lumasiran)**, an RNAi therapy for primary hyperoxaluria type 1 (PH1), was approved by the European Commission.
- **ARUVANT's ARU-1801**, a lentiviral gene therapy, was granted orphan drug designation by the European Medicines Agency (EMA) as a treatment for sickle cell disease.
- **EISAI's Fycompa (perampanel)** – This anti-epileptic was approved by the European Commission for use in children.
- **HOLOGIC's Genius Digital Diagnostics**, a cytology platform for cervical cancer screening, was granted a CE Mark.
- **INNATE PHARMA's lacutamab**, an anti-KIR3DL2 antibody for relapsed/refractory Sézary syndrome patients who have received ≥2 prior systemic therapies, was granted priority medicines (PRIME) designation by the EMA.
- **INSMED's brensocatib**, an oral DPP1 inhibitor, was granted PRIME designation by the EMA as a treatment for non-cystic fibrosis bronchiectasis.
- **ORTHO CLINICAL DIAGNOSTICS' Vitros Immunodiagnostic Products TSH3**, a reagent pack and calibrator used to diagnose thyroid and pituitary gland function, was granted a CE Mark.
- **PACIRA BIOSCIENCES' Exparel (bupivacaine liposome injectable suspension)** was approved by the European Commission as a brachial plexus block or femoral nerve block for post-operative pain.
- **SANOFI's Supemtek**, a quadrivalent recombinant influenza vaccine, was approved by the European Commission.
- **SIEMENS HEALTHINEERS' quantitative SARS-CoV-2 IgG antibody test** – which can measure the ***amount*** of antibodies in a blood sample and detect neutralizing antibodies – was granted a CE Mark.

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

- **LILLY's Emgality (galcanezumab)** – NICE is recommending use of this injectable CGRP antagonist for the prevention of migraine in adults with either chronic or episodic migraine. NICE acknowledged that the pandemic has compounded the need for migraine therapies, increased the demand for virtual appointments, and decreased the availability of AbbVie/Allergan's Botox (onabotulinumtoxinA), so a self-injected treatment like Emgality fills a need.

2020 FDA Advisory Committehes and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
November 16	**Bristol-Myers Squibb/Celgene/Juno Therapeutics' lisocabtagene maraleucel** (JCAR-017, liso-cel) for DLBCL	PDUFA date *Postponed from August 17* ***FDA said the November 16 date would be missed***
November 24	**Liquidia Technologies' LIQ-861** (inhaled dry powder treprostinil) for pulmonary arterial hypertension (PAH)	PDUFA date
November 25	**Revance Therapeutics' daxibotulinumtoxinA** for glabellar lines	PDUFA date
November 27	**Rhythm Pharmaceuticals' setmelanotide** for pro-opiomelanocortin deficiency obesity and leptin receptor deficiency obesity	PDUFA date
November 30	**Y-mAbs' naxitamab** for relapsed/refractory high-risk neuroblastoma	PDUFA date
December 2	**Coronavirus test** development and validation – another in a series of webcasts	FDA virtual Town Hall
December tba	**Pfizer and Lilly's tanezumab** to treat moderate-to-severe osteoarthritis pain	PDUFA date
December 3	**BioCryst Pharmaceuticals' Orladeyo** (berotralstat, BCX-7353) for hereditary angioedema attacks	PDUFA date
December 3	Cost barriers to **HIV PrEP** retention in care	FDA webcast
December 3	**Alnylam Pharmaceuticals' lumasiran** for primary hyperoxaluria type 1	PDUFA date
December 8	**Respirators and other PPE** for healthcare personnel during Covid-19	FDA webcast
December 10	Emergency use authorization for the first Covid-19 vaccine, **Pfizer and BioNTech's BNT162b2**	FDA's Vaccines and Related Biological Products Advisory Committee virtual meeting 9
December 11	Evaluating the **opioid REMS** on prescribing behaviors and patient outcomes	FDA virtual public workshop
December 15	**Novartis' Entresto** (sacubitril + valsartan) – expanded approval to treat heart failure with preserved ejection fraction (HFpEF)	FDA's Cardiovascular and Renal Drugs Advisory Committee *virtual meeting*
December 16	**Pfizer's Aldactone** (spironolactone) – expanded approval for treating heart failure with preserved ejection fraction (HFpEF)	FDA's Cardiovascular and Renal Drugs Advisory Committee *virtual meeting*
December 16	**Diversity** in clinical trials	FDA webcast
December 20	**FibroGen and AstraZeneca's roxadustat** for anemia of chronic kidney disease	PDUFA date
December 20	**Myovant Sciences' Relumina** (relugolix) for advanced prostate cancer	PDUFA date
December 26	**Sumitomo/Urovant Sciences' vibegron** for overactive bladder	PDUFA date
December 30	**Almirall and Athenex's tirbanibulin** (KX2-391, KX-01) for actinic keratosis	PDUFA date
2021		
January 20	**Merck MSD and Bayer's vericiguat** in HFrEF	PDUFA date
January 26	Non-clinical immunogenicity assessment of **generic peptide products**	FDA virtual public workshop
January 27	**Protalix BioTherapeutics and Chiesi's pegunigalsidase alfa** (PRX-102) for Fabry disease	PDUFA date
February 11	**Regeneron Pharmaceuticals' evinacumab** in severe homozygous familial hypercholesterolemia (HoFH)	PDUFA date
February 15	**G1 Therapeutics' trilaciclib** for small cell lung cancer	PDUFA date
February 20	**Bristol-Myers Squibb's Opdivo** (nivolumab) **+ Exelixis' Cabometyx** (cabozantinib) to treat advanced renal cell carcinoma	PDUFA date
February 28	**Roche's Gavreto** (pralsetinib) in RET-mutated medullary thyroid cancer	PDUFA date
February 28	**Regeneron Pharmaceuticals and Sanofi's Libtayo** (cemiplimab) for locally-advanced/metastatic NSCLC	PDUFA date
March 3-4	**Quality of active pharmaceutical ingredient manufacturing**	FDA webinar
March 7	**Biogen and Eisai's aducanumab** for Alzheimer's disease	PDUFA date
March 27	**Bristol-Myers Squibb and bluebird bio's idecabtagene vicleucel** (ide-cel, bb-2121), a CAR T therapy for relapsed/refractory multiple myeloma	PDUFA date
May 14	**Apellis Pharmaceuticals' pegcetacoplan** for treating paroxysmal nocturnal hemoglobinuria (PNH)	PDUFA date
May 18	**Sanofi's avalglucosidase alfa** for long-term enzyme replacement therapy for Pompe disease	PDUFA date
May 21	**ADC Therapeutics' loncastuximab tesirine** for relapsed/refractory DLBCL	PDUFA date
June 30	**Lupin Pharmaceuticals' Solosec** (secnidazole) **–** expanded approval to treat trichomoniasis	PDUFA date