TRENDS-in-MEDICINE

October 18, 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 section starts on Page 4.

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

✓ LYSOGENE's LYS-SAF302 – A patient died in a Phase II/III trial of this gene therapy in Sanfilippo syndrome type A, but it isn't known whether the death was related to the treatment.

✓ VOYAGER THERAPEUTICS' VY-HTT01 – The IND for this gene therapy for Huntington's disease was put on clinical hold by the FDA over manufacturing issues.

✓ **Positive trial news:**

- ASTELLAS and SEAGEN's Padcev (enfortumab vedotin-ejfv) – in advanced/metastatic urothelial cancer patients ineligible for cisplatin chemotherapy.
- BOEHRINGER INGELHEIM's Gilotrif (afatinib) – in squamous NSCLC patients who progressed on a PD-1 inhibitor.
- CYCLERION THERAPEUTICS IW-6463 – in age-related cognitive decline and neuro-degenerative diseases.
- GALAPAGOS and GILEAD SCIENCES' Jyseleca (filgotinib) – in ulcerative colitis.
- KYOWA KIRIN's Poteligeo (mogamulizumab-kpkc) – in mycosis fungoides and in Sézary syndrome.
- LILLY's mirikizumab – in Crohn's disease.
- MERCK MSD
  - Steglatro (ertugliflozin) – in a cardiovascular outcomes trial.
  - Zolinza (vorinostat) – in relapsed/refractory Hodgkin's lymphoma.
- REGENERON PHARMACEUTICALS and SANOFI's Dupixent (dupilumab) – in children age 6-11 with uncontrolled asthma.
- SAGE THERAPEUTICS' zuranolone – in major depressive disorder (MDD).

✓ **Negative trial news:**

- CYCLERION THERAPEUTICS' olinciguat – in sickle cell disease.
- GALAPAGOS and SERVIER's GLPG-1972/S-201086 – in knee osteoarthritis.
- GOSSAMER BIO's GB-001– in moderate-to-severe eosinophilic asthma and, in a separate trial, in chronic rhinosinusitis.
- OTSUKA/ASTEX PHARMACEUTICALS' guadecitabine (SGI-110) – in previously treated AML, myelodysplastic syndromes (MDS), or chronic myelomonocytic leukemia.
- VERTEX PHARMACEUTICALS' VX-814 – in alpha-1 antitrypsin (AAT) deficiency.

SHORT TAKES

- CARTIHEAL's Agili-C, an implant for treating cartilage lesions in arthritic and non-arthritic joints, was granted breakthrough device status by the FDA.

- INSILICO MEDICINE is collaborating with **Taisho Pharmaceutical** on research into anti-aging therapeutics.

- INVENTIVA's **lanifibranor**, a pan-PPAR agonist, was granted breakthrough therapy designation by the FDA as a treatment for non-alcoholic steatohepatitis (NASH).

- KYOWA KIRIN's Poteligeo (mogamulizumab-kpkc) – A post hoc analysis of the Phase III MAVORIC trial, presented at the European Association of Dermato Oncology virtual congress, found that higher levels of blood tumor involvement were linked to a more favorable outcome with this IgG1k anti-CCR4 antibody vs. Merck MSD's Zolinza (vorinostat) in mycosis fungoides and in Sézary syndrome.

- LYSOGENE's LYS-SAF302 – One patient died in the global Phase II/III AAVance trial of this gene therapy in Mucopolysaccharidosis Type IIIA (MPSIIIA or Sanfilippo syndrome type A), but it is not yet clear whether the death was related to the treatment.

- MALLINCKRODT, facing mounting lawsuits over both its opioid sales and its Acthar Gel (repository corticotropin injection), has filed for bankruptcy.

- NOVACYT bought **IT-IS International**, a diagnostic instrument development and manufacturing company.

- ORCA BIO's Orca-T, a cell therapy, was granted regenerative medicine advanced therapy (RMAT) designation by the FDA as a treatment for allogeneic hematopoietic stem cell transplant patients.

- OTSUKA/ASTEX PHARMACEUTICALS' guadecitabine (SGI-110) – This DNA hypomethylating agent missed the primary endpoint in the Phase III ASTRAL-2 and ASTRAL-3 trials in previously treated acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), or chronic myelomonocytic leukemia (CMML), failing to significantly improve overall survival.

- PHILOGEN's onkekafusp alpha – Swiss scientists reported in *Science Translational Medicine* that antibodies fused to either IL-12 or TNF and infused in mice slowed glioblastoma tumors, with 2 of 5 mice cured. Six months later, they infused those cured mice with glioblastoma and the mice remained healthy. The TNF/antibody treatment, now Philogen's onkekafusp alpha, was tried in three humans with glioblastoma as part of a small ongoing trial, and two remained stable for 6 months.

- POLYPHOR got a contract worth up to $18.44 million for development of a new class of antibiotics – Outer Membrane Protein Targeting Antibiotics (OMPTA) – for treating drug-resistant Gram-negative bacteria.

- REGENERON PHARMACEUTICALS and SANOFI's Dupixent (dupilumab) – In new Phase III pediatric data this anti-IL-4/13 met the primary endpoint, significantly reducing annual severe asthma attacks in children age 6-11 with uncontrolled asthma (a reduction of 59%-65% vs. placebo). Dupixent also improved lung function at Week 12 vs. placebo (10.2%-10.5% vs. 4.8%-5.3%).

- SAGE THERAPEUTICS' zuranolone (SAGE-217) – Top-line results from the ongoing Phase III SHORELINE trial showed that a 14-day course of this neuroactive steroid $GABA_A$ receptor positive allosteric modulator improved depressive symptoms in patients with major depressive disorder (MDD), with 71.6% of patients needing 1-2 treatment courses with the 30 mg dose.

- SHIONOGI's Fetroja (cefiderocol) – The results of two trials of this antibiotic were published in ***The Lancet Infectious Diseases***, offering more details on this antibiotic. In an accompanying editorial, the reviewer said the data show that cefiderocol is "as good as comparator agents that are frankly suboptimal."

- VERTEX PHARMACEUTICALS' VX-814 – A Phase II trial of this small molecule AAT corrector in patients with alpha-1 antitrypsin (AAT) deficiency was halted – and the drug abandoned – after 4 patients had ALT >8xULN, preventing the dose escalation that would have been needed to achieve efficacy.

- VOYAGER THERAPEUTICS' VY-HTT01 – The investigational new drug (IND) application for this gene therapy for Huntington's disease was put on clinical hold by the FDA, which has concerns about manufacturing issues – chemistry, manufacturing, and control (CMC).

Very early research news

- Brain tumors – Researchers at Massachusetts General Hospital reported in the journal ***Clinical Cancer Research*** that they have developed a blood test that they believe can accurately detect and monitor brain tumors by tracing two TERT gene mutations (C228T and C250T).

- Flu vaccine – Researchers reported in the journal ***Cell Systems*** on a possible strategy for a universal flu vaccine, using nanoparticles to carry flu proteins triggered by an

antibody response to the desired segment of the virus, suggesting the vaccine could be effective against any flu strain (be a universal vaccine).

- Multiple sclerosis – A study, published in the journal ***Autoimmunity Highlights***, found that a human placental extract eased clinical symptoms, inflammation, and myelin loss in a mouse model of MS, suggesting it might be useful in treating MS symptoms in people.
- Sepsis – University of Pennsylvania Perelman School of Medicine researchers reported in the journal ***Proceedings of the National Academy of Sciences*** on mast-MO, an engineered protein, derived from wasp venom that can effectively treat sepsis (at least in mice).

NEWS IN BRIEF

ASTELLAS

- and SEAGEN's Padcev (enfortumab vedotin-ejfv). The results of the pivotal, single-arm Phase II EV-201 trial in advanced/metastatic urothelial cancer patients ineligible for cisplatin chemotherapy showed a 52% objective response rate with this anti-Nectin-4 antibody-drug conjugate (ADC).
- Is buying **iota Biosciences**, a bioelectronics company that makes ultra-small medical implants.

BOEHRINGER INGELHEIM

- Gilotrif (afatinib). Data on this TKI, presented at the International Association for the Study of Lung Cancer 2020 North America Conference on Lung Cancer, included:
  - A real-world, retrospective study of patients with metastatic squamous non-small cell lung cancer (NSCLC) who progressed on first-line pembrolizumab (Merck MSD's Keytruda) which showed afatinib was a more effective second-line treatment than chemotherapy, with time-on-treatment 7.3 months vs. 4.2 months.
  - An analysis of afatinib in TKI-naïve Asian and non-Asian patients with EGFRm+ NSCLC whose tumors had G719X/L861Q/S768I non-resistant mutations from both randomized trials and real-world studies which found afatinib is as effective in NSCLC in Asians as non-Asians, with an overall response rate of 66% in Asians, 59% in non-Asians and a median duration of response 14.7 months in Asians and 15.9 months in non-Asians.
- Expanded its ongoing collaboration with **Oxford BioTherapeutics** on T cell engagers, cancer vaccines, and oncolytic viruses for treating cancer.

CYCLERION THERAPEUTICS

- Olinciguat missed the primary endpoint in a 70-patient Phase II trial in sickle cell disease. No other details were released.
- IW-6463. The company reported positive results – significant improvements in neurophysiological and objective performance measures – from a 24-subject, 15-day, crossover Phase I pharmacology (PK) trial of this sGC stimulator in age-related cognitive decline and neurodegenerative diseases, showing it could penetrate the blood-brain barrier.

GALAPAGOS

- and GILEAD SCIENCES' Jyseleca (filgotinib). Updated results from the Phase IIb/III SELECTION trial, presented at the United European Gastroenterology Week virtual conference, showed that significantly more ulcerative colitis patients taking this oral once-daily JAK1 inhibitor vs. placebo patients achieved clinical remission at Week 10 (26.1% vs. 15.3%), and those remissions were maintained through Week 58 (37.2% vs. 11.2%). In addition, significantly more filgotinib patients achieved 6-month corticosteroid-free remission (27.2% vs. 6.4%).
- and SERVIER's GLPG-1972/S-201086. This ADAMTS-5 inhibitor missed the primary endpoint in the 932-patient, 52-week, global Phase II ROCCELLA trial in knee osteoarthritis, with all three doses tested failing to reduce cartilage loss in the central medial tibiofemoral compartment vs. placebo (-0.068 to -0.097 vs. -0.116). The drug also missed all the secondary endpoints.

GOSSAMER BIO's GB-001

This oral DP2 inhibitor missed the primary endpoint in two Phase II trials:

- LEDA, a 480-patient Phase IIb trial in moderate-to-severe eosinophilic asthma, failing to significantly reduce asthma worsening vs. placebo as add-on therapy to standard of care over 24 weeks. The company was encouraged with some of the secondary endpoint data – including time to first asthma worsening. The company is still planning to move to a Phase III trial in asthma.
- TITAN, a proof-of-concept, 97-patient Phase IIa trial in chronic rhinosinusitis (with and without nasal polyps) missed the primary and secondary endpoints at Week 16. The company is ending development in chronic rhinosinusitis.

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LILLY

- Mirikizumab. New data from the Phase II SERENITY trial showed that this anti-IL-23 continued to show improvement in both endoscopic response and patient-reported outcomes (PRO) remission out to Week 52 in Crohn's disease.
- Is buying Disarm Therapeutics, which is developing SARM1 inhibitors for axonal degeneration and potentially to treat peripheral neuropathy, amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS).

MERCK MSD

- Steglatro (ertugliflozin). A study, published in the ***New England Journal of Medicine***, found that this SGLT2 inhibitor was non-inferior to placebo in reducing the risk of major adverse cardiovascular events (MACE) in Type 2 diabetics with atherosclerotic cardiovascular disease.
- Zolinza (vorinostat). A 40-patient, Phase I study, published in ***Clinical Cancer Research***, found that combining this HDAC inhibitor with an mTOR inhibitor – Novartis' Afinitor (everolimus) or Pfizer's Rapamune (sirolimus) – improved outcomes in relapsed/refractory Hodgkin's lymphoma. With sirolimus, the objective response rate was 55% and progression-free survival (PFS) 5.3 months with median follow-up of 43.3 months. With everolimus, the ORR was 33% and PFS 4.8 months with median follow-up of 21 months.

ROCHE

- Is collaborating with Dyno Therapeutics on development of gene therapy to treat central nervous system (CNS) and liver diseases, using Dyno's CapsidMap platform to develop AAV vectors.
- Is scrubbing several programs, including:
  - **RG-6000**, a DLK inhibitor for ALS.
  - **RG-7861**, an antibody-drug conjugate for *Staphylococcus aureus.*
  - **Seagen's Polivy (polatuzumab vedotin)**, an antibody-drug conjugate in follicular lymphoma.
  - **Etrolizumab** in inflammatory bowel disease, though studies are continuing in Crohn's disease.

COVID-19 WEEKLY HIGHLIGHTS

- **Politics and politicians**
  - Democratic vice presidential nominee **Kamala Harris** suspended in-person events until October 19 after two people associated with the campaign tested positive for coronavirus.
  - President Trump's son, **Barron**, had asymptomatic Covid-19 but is now negative.
  - Former New Jersey Gov. **Chris Christie** spent 7 days in an intensive care unit, suffering from Covid-19, but he is now out – and admitting it was "wrong" not to wear a mask.
- **The U.S.** In the past week, 4,905 people died from Covid-19 in the U.S.
- **The world**
  - **France** – A nightly curfew (9pm - 6am) was imposed in Paris and 5 other major cities after Covid-19 cases increased.
  - **Peru** has the highest death rate in the world from Covid-19, 105.2 per 100,000 people. This compares to 66 per 100,000 in the U.S.
- **Cruises.** Carnival Cruise Line canceled all cruises out of Florida until at least December 1 and cruises from Australia until at least January 1 (and likely until March 2021).
- **Masks.** A study by the Centers for Disease Control and Prevention (CDC) raises new questions about the role of masks. The study asked patients who tested positive as well as control patients how often they wore a mask when out in public. In the 14 days before the onset of their illness, 71% of infected patients and 74% of controls reported *always* using cloth face coverings or other mask types when in public. Another 14.5% said they *often* wore a mask.

  So, where did they get the virus? Many (42%) mask wearers had close contact with one or more persons with known Covid-19 vs. 14% of controls ($p<0.01$). Most (51%) of those close contacts were family members. So, masks may work in public, but people aren't wearing them around family members, and that's where a lot of them are getting Covid-19.

  In addition, infected patients were almost twice as likely as controls to have dined at a restaurant in the 14 days before becoming ill, though it wasn't clear if they dined inside or outside. The infected patients were also more likely to report going to a bar/coffee shop.

  Only 3.9% of respondents said they never wore face masks, but another 3.9% said they rarely did.

Re-infection. There continues to be a very small but growing number of patients with confirmed re-infection with SARS-CoV-2. Researchers are studying the patients, but there are no real conclusions yet about what this means for vaccines or transmission.

Testing

- As of October 15, the FDA had authorized 281 tests for Covid-19, including 219 molecular tests, 56 antibody tests, and 6 antigen tests. So, why is it so hard to get a rapid antigen or PCR test? Tests are available, both free and paid, but the results typically take 48-72 hours or longer.
- **Beckman Coulter** got an undisclosed grant from the Biomedical Advanced Research and Development Authority (BARDA) to develop a blood test for multisystem inflammatory syndrome in children (MIS-C), the severe childhood illness associated with Covid-19.

Transmission. A survey of >57,000 child care providers by Yale researchers, published in the journal ***Pediatrics***, found that working in child care did not increase the risk of getting Covid-19, at least in the early days of the pandemic. Fewer than half the programs stayed open or re-opened after a brief closure. About 9% of the centers closed because of a suspected or confirmed case of Covid-19.

Among the programs that continued to operate, ≥90% reported staff and children washed their hands frequently and indoor surfaces were disinfected daily, with >50% disinfecting indoor surfaces three times a day. Most programs performed daily symptom screenings and temperature checks of children and staff and practiced social distancing. However, daily face mask wearing was only 12% for children ages 2 and older and 35% for staff.

Treatment

- **AstraZeneca's AZD-7442** – The company is getting ~$486 million from BARDA to help fund two 12-month Phase III trials of this Covid-19 dual antibody treatment. One is a 5,000-person study that will test whether AZD-7442 can prevent infection, and the other is an 1,100-patient study in people who recently contracted the virus or are at high risk of exposure to see if it prevents infection *and* illness.
- **SOLIDARITY** trial – The results of this global trial of 11,266 people at 405 hospitals in 30 countries, sponsored by the World Health Organization (WHO) and published as a preprint on ***medRxiv***, found that ***none*** of the four drugs tested – Gilead Sciences' Veklury (remdesivir), hydroxychloroquine, AbbVie's Kaletra (lopinavir + ritonavir), and interferon-β1a vs. placebo – offered a mortality benefit.
- **Japan BCG Laboratory's BCG vaccine** – U.K. researchers started an international trial testing this Bacillus Calmette-Guérin vaccine in severe Covid-19 patients.
- **Lilly and AbCellera's bamlanivimab (LY-CoV-555)**
  - ✓ At the recommendation of the data safety monitoring board, the National Institute of Allergy and Infectious Diseases (NIAID) paused enrollment in the ACTIV-3 trial of this antibody + remdesivir in hospitalized Covid-19 patients after one patient had an unexplained adverse event.
  - ✓ FDA inspectors reportedly found *serious* quality control problems in the New Jersey plant where this antibody is produced, including deleted data and improperly audited data. Lilly said it has launched a "remediation" plan.
- **Prometheus** – a collaboration of academic labs, the U.S. Army Medical Research Institute of Infectious Diseases, and **Adimab** – has an antibody that isn't expected to start clinical trials until December 2020, but it is worth watching because it may be longer-acting (up to 6 months) and because it may work against a variety of coronaviruses.
- **Immune modulators** – The National Institutes of Health (NIH) has started an adaptive Phase III trial (ACTIV-1) to test three immune modulators in ~2,100 hospitalized moderate-to-severe Covid-19 patients who have a cytokine storm:
  - ✓ AbbVie's cenicriviroc, a dual CCR2/5 antagonist
  - ✓ Bristol-Myers Squibb's Orencia (abatacept), a CTLA4-IgG1
  - ✓ Johnson & Johnson's Remicade (infliximab), a TNF inhibitor

Vaccines

- **Johnson & Johnson** voluntarily halted enrollment and dosing in all of its Covid-19 vaccine studies, including the Phase III ENSEMBLE trial, so the data safety monitoring board and the company can investigate the unexplained illness of one participant.
- **Moderna's mRNA-1273** – The company started a rolling submission to Health Canada for this vaccine.
- **Pfizer and BioNTech's BNT-162b, an RNA vaccine**
  - ✓ The FDA gave the green light to enroll patients as young as 12 in the Phase III trial of this Covid-19 vaccine, and the companies increased the size of the trial from 44,000 to 48,400.

- ✓ Pfizer CEO Albert Bourla said this vaccine will not be ready to submit to the FDA for an emergency use authorization (EUA) until November 2020 (after the presidential election).

- **Russian vaccines.**
  - ✓ The government approved a second Russian Covid-19 vaccine, EpiVacCorona, a peptide vaccine, based on data on 100 volunteers, but a 30,000 post-registration trial is now planned. (The first Russian vaccine, Sputnik V, is a vector vaccine.)
  - ✓ The Russian Direct Investment Fund and Dr. Reddy's Laboratories were approved by regulators in India to conduct clinical trials in India of the Sputnik V vaccine.

- **Sanofi and Translate Bio's MRT-5500** – Positive animal data on this mRNA vaccine was posted online at ***bioRxiv***, showing it induced potent neutralizing antibodies against SARS-CoV-2. It took two doses to get antibody levels significantly higher than infected patients produced, apparently confirming this will also be a two-dose vaccine.

- **Sinovac's CoronaVac** – The future of a Phase III trial in Bangladesh is uncertain because of funding issues.

- **Vaxart's VXA-CoV2-1** – The first patients were dosed in a 48-patient Phase I trial of this recombinant vaccine, which does not have to be refrigerated. This trial is likely to determine whether this oral tablet vaccine will require one or two doses.

Vaccine issues

- **Distribution.** The Trump administration made a deal under which **CVS Health** and **Walgreens** will distribute Covid-19 vaccines to nursing homes.

- **Liability.** Vaccine manufacturers have gotten limited immunity from liability due to Covid-19 vaccine side effects, and the U.S. has a vaccine liability program, but WHO said it is still unclear what the liability issues will be in the 92 poor countries that are part of its COVAX initiative.

- **Reimbursement.** The Centers for Medicare and Medicaid Services (CMS) said it will ensure that Medicare beneficiaries get access to Covid-19 vaccines and treatments. Under current regulations, Medicare is prohibited from reimbursing for products that have an EUA instead of full FDA approval, but CMS Administrator Seema Verma said CMS is working to remove barriers to Covid-19 vaccines.

REGULATORY NEWS

Regulatory tidbits

Covid-19

- CMS added 11 telehealth services that it will cover under Medicare during the Covid-19 pandemic, including cardiac and pulmonary rehabilitation services, bringing the total of Medicare covered telehealth services to 146.

- Health and Human Services Sec. Alex Azar extended the current public health emergency in the U.S. until January 20, 2021.

FDA guidance

- The FDA issued new guidance that allows developers – during Covid-19 – to use other sample types and transport media for previously cleared respiratory syncytial virus (RSV) and influenza tests without needing to submit a 510(k) premarket notification, provided there is no undue risk.

- The FDA issued final guidance on biotin interference testing for *in vitro* diagnostic devices.

- The FDA issued and immediately implemented a new guidance on FDA clearance of molecular flu and RSV tests during the coronavirus pandemic.

FDA pilots. The FDA announced two new pilot programs:

- The Quality Management Maturity for Finished Dosage Forms Pilot Program (QMM FDF Pilot Program) for domestic drug product manufacturers of prescription and over-the-counter (OTC) drug products.

- The Quality Management Maturity for Active Pharmaceutical Ingredients Pilot Program (QMM API Pilot Program) for foreign manufacturers of APIs.

Orthopedics. CMS and the American Academy of Orthopaedic Surgeons (AAOS) will launch a bundled payment initiative in January 2021 aimed at improving decision-making through payment models for musculoskeletal care.

What's happening at the FDA?

Demy-Colton hosted a virtual Fireside Chat with Amy Abernethy, MD, PhD, principal deputy commissioner of the FDA. Among the interesting comments Dr. Abernethy made were:

- Covid-19 "doubled the workload at the FDA, and…it is really important for us to step back and follow the path we know well…but we also have to figure out where we can be flexible."

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- *Will the Covid-19 changes at the FDA continue?* "We recently embarked on a mid-pandemic review…as a way of making sure that the way we are doing our work is as efficient as possible…We are actively asking this question in a formal way." She cited three key areas the FDA learned it needs to address: regulatory flexibility, real-world data, delivery of investigational products to patients at home or somewhere near the patient.
- *What is likely to persist after the pandemic?* Real-world data, prioritizing work and resources, maintaining an urgent pace, informed drug development that helps optimize dose selection, simulated clinical trials (e.g., the simulated heart models being used to evaluate cardiac catheters).
- *What needs to change?* More digitization, so the Agency is not mired forever in paper, but, she added, "We need to continue to explain the *why*, document the science…explain that we are not lowering the evidence standard but still doing our work."
- *Will Covid-19 vaccines require a personalized medicine approach?* "Right now, none of us know how the Covid-19 story will end…It is likely there will be variety of different therapies with differing roles, depending on whether you are developing a challenge with blood clots, require oxygen…I think we will start to fit treatments together…And as vaccines get developed, which have a specific role for different populations – someone with lupus or another underlying illness [for example]…These are the kinds of questions we really need to get our heads around…Even with something approved – either an EUA or full approval – it will be important to continue to collect information on how the product is used, the safety profile, and how it is working …**We are moving to more of a cocktail personalized approach**."

FDA approvals

- ABBVIE's Venclexta (venetoclax) – The accelerated approval granted in 2018 was converted to full approval for use in combination with azacitidine, decitabine, or low-dose cytarabine in newly-diagnosed acute myeloid leukemia (AML) patients age ≥75 who have comorbidities precluding intensive induction chemotherapy.
- GE HEALTHCARE's Ultra Edition, an artificial intelligence package for its Vivid cardiovascular ultrasound systems, was granted 510(k) clearance.
- LIVMOR's Halo, a wearable atrial fibrillation detection system, was granted 510(k) clearance.
- MERCK MSD's Keytruda (pembrolizumab) was granted expanded approval for treating adults with relapsed/ refractory classical Hodgkin's lymphoma (cHL) and pediatric patients with refractory cHL or cHL that has relapsed after ≥2 lines of therapy.
- OLYMPUS AMERICA's PCF-HQ190 and PCF-H190T colonoscopes were granted 510(k) clearance.
- ORIGAMI SURGICAL's StitchKit PARK, which allows surgeons to customize the contents of the company's Stitch Kit, a suture-delivery device, with the sutures of their choice, was cleared for use.
- PRECIGEN's UltraPorator was cleared as a manufacturing device for clinical trials of the company's UltraCAR-T therapies.
- REGENERON PHARMACEUTICALS' Inmazeb (atoltivimab + maftivimab + odesivimab-ebgn) was approved to treat Ebola Zaire. This 3-antibody combination is the first FDA-approved Ebola treatment.
- SEE-MODE TECHNOLOGIES' Augmented Vascular Analysis, an artificially-run vascular ultrasound-scan software system, was granted 510(k) clearance.
- WISHBONE MEDICAL's Smart Correction, an external fixation system for use in pediatric long bone fusions, was granted 510(k) clearance.

FDA recalls/warnings

- Insulin pens – The FDA clarified revisions made in 2019 to the labeling of insulin pens, advising healthcare professionals that insulin pens should be given to patients in a sealed carton, with all the pens in that carton going to the same patient, in order to avoid usage errors.
- Optimal Health Stem Cell and Wellness Institute – Michael Johnson, DC, a neurologic chiropractor who runs this stem cell clinic in Appleton WI, received a warning letter about marketing claims for unapproved uses, including treating Parkinson's disease, MS, and traumatic brain injury.
- NSAIDs – The FDA issued a Drug Safety Communication, warning against use of non-steroidal anti-inflammatory drugs – e.g., ibuprofen, naproxen, diclofenac, and celecoxib) in the second half of a pregnancy.

European Regulatory News

- *Scotland.* NOVARTIS' Mayzent (siponimod), an S1P receptor modulator, was approved by the Scottish Medicines Consortium, to treat active secondary progressive MS.
- ADMETSYS' PrecisionOne, a system that gives real-time blood chemistry analyses and automated glucose control, was granted a CE Mark.
- CYTOSORBENTS and AFERETICA's PerLife, an integrated ex-vivo system that incorporates CytoSorbents' PerSorb sorbent cartridge and is used to perfuse, cleanse, recondition, and preserve harvested livers and kidneys, was approved for use by the European Commission.
- MICRO MEDICAL SOLUTIONS' MicroBalloon XL, a 150cm balloon catheter, and the MicroStent, a 2.5mm vascular stent, were both granted a CE Mark.
- CHMP – The EMA's Committee for Medicinal Products for Human Use recommended approval/expanded approval of 9 new drugs, approval of an interesting generic, and a marketing change for another drug:
  - AIMMUNE THERAPEUTICS' Palforzia (peanut arachis hypogaea L), an oral immunotherapy to desensitize children and adolescents to peanut allergy.
  - ALNYLAM's Oxlumo (lumasiran) to treat primary hyperoxaluria type 1.
  - ASTRAZENECA's Trixeo Aerosphere (formoterol + glycopyrronium bromide + budesonide) as maintenance therapy for chronic obstructive pulmonary disease in adults not adequately controlled.
  - GILEAD SCIENCES/KITE's Tecartus (brexucabtagene autoleucel), a gene therapy for treating relapsed/refractory mantle cell lymphoma.
  - JOHNSON & JOHNSON's Rekambys (rilpivirine) and VIIV HEALTHCARE's Vocabria (cabotegravir) – for use in combination to treat HIV-1.
  - MYLAN's Lenalidomide Mylan (generic lenalidomide) to treat multiple myeloma and follicular lymphoma.
  - NOVARTIS' Leqvio (inclisiran) to treat primary hypercholesterolemia or mixed dyslipidemia.
  - ORCHARD THERAPEUTICS' Libmeldy (cryopreserved autologous CD34+ cells encoding the *arylsulfatase-A*, or *ARSA*, gene), a gene therapy for treating children with "late infantile" or "early juvenile" forms of metachromatic leukodystrophy.
  - RATIOPHARM's desloratadine – CHMP recommended removing the requirement for a prescription for this allergy drug but to limit it to adults and to restrict the urticaria indication to chronic idiopathic urticaria.
  - REGENERON PHARMACEUTICALS and SANOFI's Dupixent (dupilumab) – expanded approval to include children age 6-11 with severe atopic dermatitis (AD) who are candidates for systemic therapy. This would be the first biologic approved in the European Union to treat these children.
  - ZOGENIX's Fintepla (fenfluramine) for treating seizures associated with Dravet syndrome.

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

- NOVARTIS' Mayzent (siponimod) – NICE recommended approval of this S1P receptor modulator to treat secondary progressive multiple sclerosis (SPMS) after the company offered an undisclosed price discount.
- SANOFI's Sarclisa (isatuximab) – NICE recommended approval of this anti-CD38 in combination with pomalidomide (Bristol-Myers Squibb/Celgene's Pomalyst) and dexamethasone (PomDex) – as a ≥4-line treatment for relapsed/refractory multiple myeloma.

Regulatory news from other countries

- *Japan.* CHUGAI's Evrysdi (risdiplam) – A new drug application was submitted for this oral therapy for spinal muscular atrophy.

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2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
October 7	**TransMedics' TransMedics Organ Care System** (OCS) **Heart** – normothermic heart transplant transport	FDA's Circulatory System Devices Advisory Committee virtual meeting **Postponed indefinitely by the FDA**
October 19	Digital Health Center of Excellence **Listening Session #1**	FDA webcast
October 19-20	Updates on ongoing research to address challenges of **generic drug-device combination products**	FDA and Drug Information Agency (DIA) Generic Drug-Device Combination Products *virtual* Conference
October 21	Discussion of technical questions about **SARS-CoV-2 test development**	FDA virtual Town Hall for test developers
October 22	**Covid-19 vaccines** general discussion	FDA's Vaccines and Related Biological Products Advisory Committee virtual meeting
October 22	**Artificial intelligence** and machine learning in medical devices	FDA's Patient Engagement Advisory Committee virtual meeting
October 22	Conversation on Cancer: Building connections toward **Native American** trial participants	FDA's Oncology Center of Excellence webcast
October 22-23	Pediatric **dose selection**	FDA virtual public workshop
October 24	**Spectrum Pharmaceuticals' Rolontis** (eflapegrastim) for treating chemotherapy-induced neutropenia	PDUFA date
October 25	**Regeneron Pharmaceuticals' REGN-EB3** for Ebola	PDUFA date
October 27	Antimicrobial drugs to treat **gonorrhea**	FDA virtual public workshop *Postponed from August 21*
October 27	**Medical device user fee** amendments for fiscal years 2023-2027	FDA virtual public meeting
October 27	**Neovasc's Neovasc Reducer System** for treating refractory angina pectoris	FDA's Circulatory System Devices Advisory Committee virtual meeting
October 27-28	**Orange Book Conference**	FDA webcast
October 30	Integrated assessment of **marketing applications**	FDA virtual public workshop
November 2	Sentinel Initiative on **maternal health and pregnancy**	FDA virtual training session
November 2	**Olas Pharma's Hydexor** (hydrocodone + acetaminophen + promethazine) for acute post-operative pain	FDA's Anesthetic and Analgesic Drug Products Advisory Committee virtual joint meeting with the Drug Safety and Risk Management Advisory Committee
November 6	**Biogen and Eisai's aducanumab** in Alzheimer's disease	FDA's Peripheral and Central Nervous System Drugs Advisory Committee virtual meeting
November 9	**ReFocus Group's VisAbility Micro Insert** for presbyopia	FDA's Ophthalmic Devices Advisory Committee virtual meeting
November 12	Digital Health Center of Excellence **Listening Session #2**	FDA webcast
November 13	**Orthopedic device-related infections**	FDA virtual public workshop
November 13	Promoting safe and effective prescription drug use in **geriatric patients**	FDA webinar
November 15	**Alkermes' ALKS-3831** (olanzapine + samidorphan) for bipolar I disorder and schizophrenia	PDUFA date
November 16	**Bristol-Myers Squibb/Celgene/Juno Therapeutics' lisocabtagene maraleucel** (JCAR-017, liso-cel) for DLBCL	PDUFA date *Postponed from August 17*
November 16	Ranking of **antimicrobial drugs** by importance in human medicine	FDA virtual public meeting by the FDA's Center for Veterinary Medicine
November 17	**Safety of medical devices**	FDA virtual public meeting
\November 19	**CBD and other cannabinoids** – sex and gender differences in use and response	FDA's Office of Women's Health virtual Scientific Conference
November 19	Reauthorization of the **Biosimilar User Fee Act** (BsUFA) for FY2023-2027	FDA virtual public meeting
November 20	**Eiger BioPharmaceuticals' Zokinvy** (lonafarnib) for progeria and progeroid laminopathies	PDUFA date
November 25	**Revance Therapeutics' daxibotulinumtoxinA** for moderate-to-severe glabellar lines	PDUFA date
November 27	**Rhythm Pharmaceuticals' setmelanotide** for pro-opiomelanocortin deficiency obesity and leptin receptor deficiency obesity	PDUFA date

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more - 2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
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	**Alnylam Pharmaceuticals' lumasiran** for primary hyperoxaluria type 1	PDUFA date
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 Dainippon Pharma/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 28	**Roche's Gavreto** (pralsetinib) in RET-mutated medullary thyroid cancer	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