TRENDS-in-MEDICINE

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by Lynne Peterson

Quick Takes

…Highlights from this week's news relating to drugs and devices in development that are not covered in other *Trends-in-Medicine* reports…

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NOTE: The Covid-19 section starts on Page 5. Subscribe to ***Trends-in-Medicine*** for our coverage of the virtual Dry AMD Therapeutic Development Summit and the Covid-19 discussion at the virtual meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP).

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

- ✓ GILEAD SCIENCES and GALAPAGOS' filgotinib – Enrollment was paused in 3 trials in response to the FDA's rejection in rheumatoid arthritis due to safety concerns.
- ✓ NEOVASC's Neovasc Reducer System – An FDA advisory committee voted 13-3 that the benefits of this angina pectoris device do not outweigh the risks.
- ✓ ULTRAGENYX PHARMACEUTICAL and GENETX BIOTHERAPEUTICS' GTX-102 – A trial in Angelman syndrome was paused after 2 patients temporarily lost the ability to walk.
- ✓ **Positive trial news:**
  - ABBVIE/ALLERGAN's AGN-190584 (pilocarpine 1.25%) – in presbyopia.
  - ASTRAZENECA's Fasenra (benralizumab) – in elimination of oral corticosteroids in steroid-dependent asthma patients.
  - AXOVANT GENE THERAPIES' AXO-Lenti-PD – in Parkinson's disease.
  - CONNECT BIOPHARMA's CBP-201 – in atopic dermatitis symptoms.
  - CRINETICS PHARMACEUTICALS' paltusotine – in acromegaly.
  - FORMA THERAPEUTICS' olutasidenib – in relapsed/refractory acute myeloid leukemia (AML).
  - MAGNOLIA MEDICAL TECHNOLOGIES' Steripath Gen2 Initial Specimen Diversion – in sepsis testing.
  - REGENERON PHARMACEUTICALS and SANOFI's Dupixent (dupilumab) – in eosinophilic esophagitis.
  - SANOFI's olipudase alfa – in Niemann-Pick disease.
  - SCHOLAR ROCK's SRK-015 – in spinal muscular atrophy (SMA) types 2 and 3.
  - TAKEDA's TAK-721 (budesonide oral suspension, BOS) – in eosinophilic esophagitis.
  - UCB's bimekizumab – in moderate-to-severe psoriasis.
- ✓ **Negative trial news:**
  - BELLICUM PHARMACEUTICALS' BPX-601 – in relapsed/ refractory metastatic pancreatic cancer.

- BIONDVAX PHARMACEUTICALS' M-001 – a universal flu vaccine.
- CATABASIS PHARMACEUTICALS' edasalonexent (CAT-1004) – in Duchenne muscular dystrophy (DMD).
- MERCK MSD and BAYER's vericiguat – in heart failure with preserved ejection fraction (HFpEF).

SHORT TAKES

- ABBVIE/ALLERGAN's AGN-190584 (pilocarpine 1.25%) – This cholinergic muscarinic receptor agonist met the primary endpoint in two Phase III trials – GEMINI-1 and GEMINI-2 – in presbyopia patients gaining ≥3 lines of vision in low light. Most secondary endpoints were also met, and there were no serious treatment-related adverse events.

- ANAPTYSBIO and **GlaxoSmithKline** amended their collaboration agreement in immuno-oncology, which, among other things, gives AnaptysBio a higher royalty on Zejula (niraparib) and dostarlimab and gives GSK the right to develop and commercialize Zejula in combination with third party molecules.

- APELLIS PHARMACEUTICALS' pegcetacoplan was partnered with **Swedish Orphan Biovitrum** (Sobi) on this Complement C3 inhibitor in hematology, nephrology, and neurology. Sobi got co-development and exclusive non-U.S. commercialization rights for systemic use, and Apellis keeps the U.S. commercialization rights for systemic use as well as the worldwide rights in geographic atrophy (GA).

- ASTELLAS' ASP-8374 (PTZ-201) – Development was discontinued of this anti-TIGIT antibody, obtained with the purchase of Potenza Therapeutics, after it failed to show benefit in a Phase I trial.

- BAYER is buying **Asklepios BioPharmaceutical** (AskBio), which is working on AAV-based gene therapies in several therapeutic areas.

- BIONDVAX PHARMACEUTICALS' M-001, a universal flu vaccine, missed the primary endpoint in a pivotal 12,463-patient Phase III trial in Eastern Europe, with no significant difference vs. placebo in reduction in flu illness or the severity of disease vs. placebo.

- BRISTOL-MYERS SQUIBB is collaborating with **insitro** in a 5-year deal on discovery and development of treatments for amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD).

- CATABASIS PHARMACEUTICALS' edasalonexent (CAT-1004) missed the primary endpoint in the 1-year, 131-patient Phase III PolarisDMD trial in Duchenne muscular dystrophy (DMD), failing to beat placebo on the North Star Ambulatory Assessment (NSAA). Edasalonexent also missed the secondary endpoint (timed function tests), though it was generally safe and well-tolerated. As a result, the company is stopping development of edasalonexent, including the ongoing GalaxyDMD open-label extension trial.

- CONNECT BIOPHARMA's CBP-201 – The completed Phase Ib trial data, presented at the European Academy of Dermatology and Venereology (EADV) virtual meeting, showed that this IL-4Rα inhibitor was well tolerated out to Week 11, with rapid, early, and continued improvement in atopic dermatitis symptoms.

- CRINETICS PHARMACEUTICALS' paltusotine met the primary endpoint in a Phase II trial as maintenance therapy for acromegaly, maintaining IGF-1 levels over 13 weeks. Safety also looked acceptable.

- EISAI expanded its collaboration with **Cogstate**, getting all global rights to development and commercialization of any cognitive function tests developed by Cogstate, including the Cogstate Brief Battery (CBB), a scientifically validated digital tool that enables cognitive function self-checks. CBB consists of four tests that evaluate psychomotor function, attention, learning and memory, and working memory.

- EXACT SCIENCES is buying **Thrive Earlier Detection**, which has cancer screening liquid biopsy technology.

- FORMA THERAPEUTICS' olutasidenib, an IDH1m inhibitor, met the primary endpoint in the 500-patient, open-label Phase II FT2102-HEM-101 trial in relapsed/refractory acute myeloid leukemia (AML), with a complete remission rate of 30% in the 123 patients with an IDH1 mutation.

- GILEAD SCIENCES and GALAPAGOS' filgotinib – Gilead paused enrollment in three trials of this JAK1 inhibitor – a Phase III trial in psoriatic arthritis, a Phase III trial in ankylosing spondylitis, and a Phase II trial in uveitis – in response to the FDA's decision in August 2020 to reject a new drug application (NDA) in rheumatoid arthritis, citing safety concerns.

- GLAXOSMITHKLINE's GSK-3772847 – Development in asthma of this IL-33 inhibitor, obtained from Johnson & Johnson, was discontinued.

- INTERMOUNTAIN HEALTHCARE is merging with **Sanford Health**, a rural hospital system with operations in 24 states.

- MAGNOLIA MEDICAL TECHNOLOGIES' Steripath Gen2 Initial Specimen Diversion, a blood culture contamination device, showed positive results in sepsis testing, with no false-positive central line-associated bloodstream infections and no blood culture contamination events vs. traditional methods, which had a contamination rate of 3.15%.

- MEDTRONIC bought **Ai Biomed**, which gives it PTeye, a tissue-detecting laser probe for use in thyroid surgery

- MERCK MSD and BAYER's vericiguat – In the 789-patient Phase IIb VITALITY-HFpEF trial, published in ***JAMA***, this oral soluble guanylate cyclase stimulator failed to significantly improve KCCQ physical limitation scores at Week 24 in patients with worsening heart failure with preserved ejection fraction (HFpEF).

- NEOVASC's Neovasc Reducer System – The FDA's Circulatory System Devices Advisory Committee voted 14-4 in a virtual meeting that this device for treating refractory angina pectoris is safe but didn't think it works, voting 1-17 that it is effective. The panel also voted 13-3 (with 2 abstentions) that the benefits do not outweigh the risks.

- NEUROEM THERAPEUTICS' Memorem, a wearable head transcranial electromagnetic treatment (TEMT) device for treating Alzheimer's disease, was granted breakthrough device status by the FDA.

- NOVO NORDISK's NN-9828 – Development of this IL-21 inhibitor for Type 1 diabetes – with or without Victoza (liraglutide) – was discontinued.

- SCHOLAR ROCK's SRK-015 – In an interim analysis at 6 months in the 12-month Phase II TOPAZ trial in spinal muscular atrophy (SMA) types 2 and 3, this myostatin inhibitor significantly improved motor function (+2.4 points on the Hammersmith scale with the low dose). In the analysis, 67% of patients had ≥1 point improvement.

- SPRINGWORKS THERAPEUTICS' PF-04457845, an FAAH inhibitor, was licensed to **Jazz Pharmaceuticals**, which plans to develop it to treat post-traumatic stress disorder (PTSD).

- SURGALIGN bought **Holo Surgical**, the developer of the ARAI surgical navigation system.

- SYNEOS HEALTH is buying **Synteract**, a contact research organization (CRO).

- TELEFLEX is buying **Z-Medica**, which makes hemostatic products.

- ULTRAGENYX PHARMACEUTICAL and GENETX BIOTHERAPEUTICS' GTX-102 – A 5-patient Phase I/II trial of this antisense oligonucleotide in Angelman syndrome was paused after all 5 patients (1 at the second highest dose and 4 at the highest dose) had lower extremity weakness and two of these patients temporarily lost the ability to walk. The company plans to amend the dosing regimen. Despite this, the companies claimed the interim data were positive, with all patients having improvement in ≥2 disease domains.

- UNUM THERAPEUTICS changed its name to **Cogent Biosciences**.

- VERASTEM ONCOLOGY's VS-6766 (CH-5126766) – An investigator-initiated Phase I study, published in ***Lancet Oncology***, showed that this RAF/MEK inhibitor, given with an intermittent dosing schedule (4 mg BIW), is tolerable, with antitumor activity in RAS-mutant tumors.

- VIRTUAL INCISION's MIRA – The FDA approved an investigational device exemption (IDE) application for this miniaturized robot-assisted surgery platform.

- XERIS PHARMACEUTICALS' XP-0863, a diazepam nonaqueous injection, was granted fast track status by the FDA as a treatment for acute repetitive seizures.

Very early research news

- Neurology – A mouse study by researchers at Ohio State University and the University of Michigan, published in ***Nature Immunology***, suggests that a new type of immune cell can rescue damaged nerve cells and partially reverse nerve fiber damage. The discovery could lead to new treatments for degenerative neurological diseases such as amyotrophic lateral sclerosis (ALS) and multiple sclerosis, stroke, and spinal injuries.

- Pancreatic cancer – A study by Fox Chase Cancer Center researchers, published in the journal ***Cancer Discovery***, has identified a new biomarker – and a potential novel treatment target – for pancreatic ductal adenocarcinoma (PDAC). The target is Netrin G1 (NetG1), a brain synaptic protein ectopically expressed in the fibroblastic cells of the pancreas.

NEWS IN BRIEF

ASTRAZENECA

- and DAIICHI SANKYO's Enhertu (fam-trastuzumab deruxtecan-nxki) was granted priority review by the FDA as a treatment for HER2+ metastatic gastric cancer.

- Atacand (candesartan cilexetil) and Atacand Plus (candesartan cilexetil and hydrochlorothiazide). The rights to

these anti-hypertensive/heart failure drugs were sold to **Cheplapharm Arzneimittel**.

- Fasenra (benralizumab). This IL-5 inhibitor met the primary endpoint in the Phase IIIb PONENTE trial in oral corticosteroid (OCS)-dependent asthma, with 62% of Fasenra patients able to eliminate daily OCS use. The key secondary endpoint was also met, with 81% of Fasenra patients able to either eliminate daily OCS use or reduce it to ≤5 mg. Both results were maintained ≥4 weeks.
- Imfinzi (durvalumab). In a collaboration with **Arcus Biosciences**, this anti-PD-L1 will be tested with Arcus' anti-TIGIT, domvanalimab, in unresectable Stage III non-small cell lung cancer (NSCLC).

AXOVANT GENE THERAPIES' AXO-Lenti-PD

- The second cohort of the Phase II SUNRISE-PD trial in Parkinson's disease, at 6 months, showed good safety and tolerability, improvement in both ON and OFF time, improvement in the UPDRS Part II and Part III OFF scores in 2 evaluable patients, and a reduction in levodopa-equivalent daily dose.
- Reported that development of a suspension-based manufacturing process for this gene therapy will take longer than expected due to manufacturing issues encountered by manufacturing partner, **Oxford Biomedica**.

BELLICUM PHARMACEUTICALS

- BPX-601. In interim data from a dose-escalation study in patients with relapsed/refractory metastatic pancreatic cancer, there was no meaningful efficacy by RECIST. And there was a case of cytokine release syndrome in one patient. However, the company said it is not giving up on BPX-601.
- BCMA GoCAR-NK. This natural killer cell therapy program that targets B-cell maturation antigen in hematologic cancers is being "paused" to conserve funds to continue development of BPX-601 and BPX-603.

DASSAULT SYSTÈMES/MEDIDATA

- Is collaborating with **TriNetX** and **Datavant** to bolster use of real-world data in clinical drug development.
- Bought **MC10**, a digital biomarker business.

NOVARTIS

- Is collaborating with **Molecular Partners** on two preclinical tri-specific DARPins – MP-0420 and MP-0423 – as potential treatments for Covid-19.
- Bought **Vedere Bio**, which is developing intravitreally-injected AAV gene therapies for vision restoration.

PFIZER

The company ended development of three drugs:

- **PF-05221304**, an acetyl-CoA carboxylase inhibitor for non-alcoholic steatohepatitis (NASH).
- **PF-06650833**, an IRAK4 inhibitor for arthritis.
- **PF-06753512**, a prostate cancer therapeutic vaccine.

REGENERON PHARMACEUTICALS and SANOFI

- Dupixent (dupilumab)
  - Part A of an 81-patient pivotal Phase III trial, presented at the American College of Gastroenterology (ACG) virtual meeting, showed that patients with eosinophilic esophagitis (EoE) taking this IL-4R inhibitor had significantly improved ability to swallow vs. placebo as early as Week 4 that continued to improve out to Week 24.

    Dupixent patients also had significantly improved structural esopha-geal abnormalities vs. placebo. In addition, Dupixent patients had a normalization of the gene expression pattern associated with type 2 inflammation.
  - In atopic dermatitis studies presented at EADV, Dupixent showed long-term efficacy and high patient satisfaction, rapid improvement in itch and sleep, and long-term safety.
- Libtayo (cemiplimab-rwlc). This PD-1 inhibitor was granted priority review as a first-line treatment for locally advanced/metastatic non-small cell lung cancer with PD-L1 expression ≥50%. The PDUFA date is February 28, 2021.

SANOFI

- Olipudase alfa. In two studies (ASCEND and ASCEND-Peds), presented at the American Society of Human Genetics (ASHG) virtual meeting, this recombinant human acid sphingomyelinase significantly improved lung function and spleen volume in patients with acid sphingomyelinase deficiency (Niemann-Pick disease) – -39.5% vs. +0.5% with placebo.
- THOR-707, a non-alpha IL-2 it got with the purchase of Synthorx, will be tested in various cancers in combination with a PD-1 inhibitor, Keytruda (pembrolizumab), in a collaboration with **Merck MSD**.

TAKEDA

- **TAK-721 (budesonide oral suspension, BOS).** Post hoc analyses from a 12-week Phase III trial in eosinophilic esophagitis, presented at the ACG meeting, showed this oral mucoadherent topical corticosteroid safely improved endoscopic and histologic response.
- Is collaborating with **Seqster** for use of its secure platform in collecting real-world data – electronic health records, genomic profiles, and wearable data.

UCB's bimekizumab

Post hoc analyses of the Phase III BE SURE and BE VIVID trials, presented at the EADV meeting, showed that this IL-17AF inhibitor was *superior* to AbbVie's Humira (adalimumab), a TNF inhibitor, in patients with moderate-to-severe psoriasis:

- In BE SURE at Week 16, significantly more bimekizumab patients achieved PASI100 (60.8% vs. 23.9%, PASI90 (86.2% vs. 47.2%), and IGA 0/1 (85.3% vs. 57.2%).
  - ✓ The differences were apparent early and continued out to Weeks 16, 24, and 56.
  - ✓ Q8W dosing was effective.
- In BE VIVID, bimekizumab showed remarkable results vs. Johnson & Johnson's Stelara (ustekinumab), an anti-IL-12/23, in very hard to treat locations – PASI100 scalp at Week 16 (75.7% vs. 58.8%) and palmoplantar at Week 52 (64.5% vs. 38.0%).

Why is another psoriasis drug interesting? A survey of 8,338 psoriasis patients found that 57% had not achieved self-assessed clear/almost clear skin with existing drugs, and more than half of those were not aware it was even possible to achieve clear/almost clear skin.

COVID-19 WEEKLY HIGHLIGHTS

- **The numbers:**
  - **Worldwide** – more than 46 million cases, with 1.2 million deaths, a fatality rate of 16 per 100,000.
  - **U.S.** – more than 9.2 million cases, with 231,000 deaths, a fatality rate of 70 per 100,000. Former FDA Commissioner Scott Gottlieb, MD, warned that the U.S. is only at "the beginning of the steep part" of the pandemic, and Anthony Fauci, MD, director of the National Institute for Allergy and Infectious Diseases (NIAID), said, "We're in for a whole lot of hurt. It's not a good situation…All the stars are aligned in the wrong place…You could not possibly be positioned more poorly."
  - **U.K.** – 1 million cases, with 46,717 deaths, a fatality rate of 70 per 100,000.
  - **Europe** – 11 million cases, with 285,000 deaths, a fatality rate of 38 per 100,000.
- **The world**
  - The situation has worsened so much that Prime Minister Boris Johnson issued a month-long stay-at-home (lockdown) order in **England**.
  - **Italy, Germany, and France all have or are imposing** new restrictions. In Italy, the number of patients in intensive care now matches the rate in March 2020.
  - **Russia** mandated masks.
- **Cruises.** The CDC issued the framework for cruise lines to resume operations. It's a phased approach which emphasizes preventing ships from spreading the virus to U.S. communities. But, and it is a big but, those phases don't look easy, inexpensive, or quick to accomplish. They include testing crew members, ensuring adequate health and safety protections for crew members, laboratory capacity to test passengers, conduct test sailings (cruises without passengers or with "volunteer" passengers without pre-existing conditions). *Bottom line:* Don't plan to take a cruise any time soon unless you want to be a guinea pig.
- **Immunity.** A U.K. study by Imperial College London researchers and Ipsos MORI, a market research company, showed evidence that immunity to Covid-19 wanes gradually, with >26% decline over the first 3 months after recovery, similar to seasonal coronaviruses. In June, at the beginning of the study, 6% of those tested had IgG antibody responses to the coronavirus, but by September, only 4.4% of them did. On the other hand, other experts have pointed out that if immunity wanes this quickly, there ought to be more reports of re-infections, and so far there are only a handful of cases worldwide.
- **Infectivity.** A study by **Regeneron Pharmaceuticals**, presented at the American Society of Human Genetics virtual meeting found four gene locations and three specific genes that make people more susceptible to Covid-19 and more likely to get severe disease.
- **Treatments**
  - **Boehringer Ingelheim's BI-764198**, a TRPC6 inhibiter, a kidney drug, will now be tested in Covid-19.

- **Evgen Pharma's SFX-01** was given the go-head from U.K. regulators to start a trial of this sulforaphane as a treatment for acute respiratory distress syndrome (ARDS) in patients suspected of having Covid-19.
- **Lilly's LY-CoV555**
  - ✓ NIAID ended a trial of this antibody as a treatment for hospitalized Covid-19 patients after determining that the drug was ineffective at improving their condition.
  - ✓ Despite those trial results, the government gave Lilly a $375 million deal to provide the antibody.
  - ✓ The detailed results of the BLAZE-1 trial of this antibody, published in the ***New England Journal of Medicine*** – and the basis of the FDA filing for an emergency use authorization (EUA) for the low dose (700 mg). But viral levels fell 0.53 vs. placebo (p=0.02) with the 2800 mg dose but only fell 0.20 with the 700 mg dose (p=0.38).
- **Lilly's Evista (raloxifene)** – Researchers in Italy have gotten the go-ahead for a trial of generic raloxifene to treat Covid-19, based on a prediction from a supercomputer that screened >400,000 molecules searching for treatment candidates.
- **Regeneron Pharmaceuticals' REGN-COV2**
  - ✓ At the recommendation of the independent data safety monitoring committee, enrollment was halted in a trial of this dual antibody cocktail in patients on high-flow oxygen or mechanical ventilation. The issue is a potential safety signal and an "unfavorable risk:benefit profile." No details on that safety issue were disclosed. Enrollment in the trial is continuing for hospitalized patients who don't require oxygen or require only low-flow oxygen.
  - ✓ Data on an additional 524 patients for the ongoing Phase II/III trial showed this antibody cocktail met the primary and key secondary endpoints, significantly reducing viral load and patient medical visits (hospitalizations, emergency room visits, urgent care visits, or physician office/telehealth visits).

Vaccines

- The **FDA** said it will not require manufacturing site inspections for an EUA.
- **Canada** is investing >$162 million to support development of a domestic Covid-19 vaccine. Two recipients: **Medicago** and **Precision NanoSystems**.
- **Cadila Healthcare** is looking for partners to help produce up to 70 million doses of its Covid-19 vaccine, which is currently in a Phase II trial.
- **Novavax** is delaying the start of a Phase III trial in the U.S. of its Covid-19 vaccine until the end of November due to issues with scaling up manufacturing.
- **Pfizer** CEO Albert Bourla, DVM, PhD, had promised to release data on its vaccine by the end of October, but the company reportedly hasn't even done its interim analyses yet, and there won't be a data release until late this month (at the earliest).

REGULATORY NEWS

Regulatory tidbits

CDC. The Centers for Disease Control and Prevention launched Project Firstline, a $180 million infection control program designed to help prevent the spread of infectious diseases (all of them, not just Covid-19) in U.S. healthcare settings. The program includes new training for staff in hospitals, outpatient clinics, dialysis centers, nursing homes, and other healthcare facilities.

CMS. The Centers for Medicare and Medicaid Services finalized a rule that forces employer health plans and insurance companies to post in-network and out-of-network rates they negotiate with providers. It also requires insurers to develop online price transparency tools to give patients cost-sharing information.

Florida drug imports. No private firms bid on Florida's $30 million contract to set up and operate a drug importation program, which is likely to delay by at least several months Florida's effort to become the first state to import drugs. Florida's Agency for Health Care Administration said it is exploring options and is still looking for a qualified vendor.

FDA

- **Compounded drugs.** The FDA issued a memorandum of understanding (MOU) between the FDA and the states on interstate distribution of compounded drugs. States have 1 year to agree to the MOU or they will be banned from distribution of >5% of a compounded drug in *other* states.
- **Covid-19**
  - ✓ **Antigen tests** – The FDA updated its Antigen Template for Test Developers, which provides the FDA's current recommendations on data and information that should be submitted to the FDA in support of an emergency authorization request for a SARS-CoV-2 antigen test.

- ✓ **Oxygen** – The FDA issue an update to provide consumers with more information about at-home pulse oximeters and at-home oxygen therapy.
- ✓ **Remote monitoring devices** – The FDA updated its enforcement policy for non-invasive remote monitoring devices used to support patient monitoring during the Covid-19 pandemic to include gaseous-phase carbon-dioxide gas analyzers, including capnographs and devices with a capnography feature.

- **Essential drugs**. The FDA issued an updated list of essential medicines. On the list: 223 drugs and biological products and 96 medical devices.

- **Generic drugs**
  - ✓ A study by researchers at the FDA's Center for Drug Evaluation and Research (CDER) found that an abbreviated new drug application (a generic application) was filed within two weeks of the end of brand drug exclusivity more than half the time.
    - ➢ ANDAs were 4-times more likely to occur if the brand-name drug had generated high revenues (e.g., >$250 million/year for 4 years) vs. $10 million/year.
    - ➢ An ANDA was less likely if the drug was classified as "complex."
    - ➢ ANDAs were more common for drugs with product-specific guidance already published.
  - ✓ The FDA said that real-world evidence, like clinical trial data, confirms that generic drugs are therapeutically equivalent to brand-name drugs.

- **Illegal drugs.** The FDA is working with U.S. Customs and Border Protection (CBP), Immigration and Customs Enforcement (ICE), and the Department of Homeland Security (DHS) in a effort to prevent the importation of illegal and harmful medical products through international mail.

- **Reference drugs.** The FDA issued final guidance for generic drugmakers on the identification of reference listed drugs for abbreviated new drug applications (ANDAs).

- **Returned drugs.** The FDA postponed until November 27, 2023, enforcement of a part of the Drug Supply Chain Security Act that requires wholesale distributors to verify returned drugs that they plan to distribute further.

■ ONC. The Office of the National Coordinator for Health Information Technology (ONC) issued an interim final rule that delays compliance deadlines with interoperability until at least 2021.

FDA approvals/clearances

■ ABIOMED's Breethe OXY-1, an all-in-one compact cardiopulmonary bypass system, was granted 510(k) clearance.

■ AVIOQ's VioOne, an HIV Profile Supplemental Assay, was cleared for use.

■ C4 IMAGING's Multimodality C4 Fiducial Marker, a non-metallic implantable MRI marker, was granted 510(k) clearance.

■ DIA IMAGING ANALYSIS' LVivo Seamless, which aids in the automatic view selection of cardiac ultrasound views, was granted 510(k) clearance.

■ EMBODY's Tapestry, a biointegrative implant for tendon and ligament repair, was granted 510(k) clearance.

■ KALA PHARMACEUTICALS' Eysuvis (loteprednol etabonate ophthalmic) was approved for the short-term (≤2 week) treatment of the signs and symptoms of dry eye disease.

■ MEDTRONIC
- Abre, a venous self-expanding stent system for use in patients with symptomatic iliofemoral venous outflow obstruction, was cleared for use.
- NIM Vital, a nerve monitoring system, was granted 510(k) clearance.

■ NVISION's Trigon Osteotomy Wedge, an implant for promoting bone fusion, was granted 510(k) clearance.

■ ROCHE's cobas EGFR Mutation Test v2 was approved as a companion diagnostic for NSCLC therapies.

■ SIEMENS HEALTHINEERS' YSIO X.pree, a ceiling-mounted radiography (x-ray) system, was cleared for use.

■ VIDA DIAGNOSTICS' LungPrint solution, an artificial intelligence-based lung imaging analysis software, was granted 510(k) clearance.

FDA recalls/warnings

■ BAXTER's Sigma Spectrum Infusion Pumps (V6, V8, and IQ) – The company issued an Urgent Device Correction to reinforce safety information about the appropriate cleaning practices for these devices, warning that deviations from the specified cleaning methods may impair infusion pump functionality and performance.

■ Covid-19
- The FDA issued warning letters to two companies for distributing chloroquine phosphate products for aquarium fish to humans – **Everything Aquatic** and **Mr Frags**.

- The FDA and the Federal Trade Commission jointly sent warning letters to three companies for selling unapproved and misbranded products with fraudulent Covid-19 claims: **Peterson Research Laboratories** (dba Covercology), **Predator Nutrition**, and **Beepothecary**.

- KVK-TECH received its *second* warning letter this year for the same thing – for improper cleaning procedures at its Pennsylvania plant.
- SHILPA MEDICARE, a drug manufacturer in India, received a warning letter for failing to notify the FDA *multiple* times about issues with its sterile injectables.
- SUNSTAR AMERICAS' Paroex (chlorhexidine gluconate), an oral rinse, was recalled due to microbial contamination.

European Regulatory News

- GLAXOSMITHKLINE's Zejula (niraparib), a once-daily PARP inhibitor, was approved by the European Commission as a first-line maintenance treatment for women with advanced epithelial high-grade ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) following completion of platinum-based chemotherapy, regardless of biomarker status.
- MMI's Symani, a surgical system used for robotic microsurgery, was granted a CE Mark.
- PERKINELMER's PKamp, a respiratory SARS-CoV-2 RT-PCR test that can also detect and differentiate between influenza A and B, respiratory syncytial virus, and SARS-CoV-2, was granted a CE Mark.
- ROCHE's Tecentriq (atezolizumab) was approved by the European Commission for use in combination with Avastin (bevacizumab) to treat unresectable hepatocellular carcinoma (HCC).

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

- BIOGEN's Spinraza (nusinersen) – NICE has started a review of this treatment for spinal muscular atrophy to see if type 3 patients unable to walk unaided should be included in the conditional reimbursement program that will fund the therapy until at least July 2024.
- Covid-19 – NICE, in cooperation with the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners are working on guidelines for treatment of the persistent effects of Covid-19 (Long Covid) on patients.
- NOVO NORDISK's Saxenda (liraglutide) – NICE recommended use of this GLP-1 by adults with non-diabetic hyperglycemia with a body mass index (BMI) of ≥35 and high-risk cardiovascular disease.

Regulatory news from other countries

- ***China.*** ROCHE's Tecentriq (atezolizumab) was approved in combination with Avastin (bevacizumab) to treat unresectable hepatocellular carcinoma.
- ***Singapore.*** SANOFI's VaxigripTetra and SK BIOSCIENCE's SKYCellflu – Use of both of these flu vaccines was temporarily halted by the Ministry of Health because they are among the 7 flu vaccines used in South Korea that were tied to deaths there.
- ***South Korea.*** *Flu vaccines* – As of October 29, there have been 72 deaths following flu vaccinations in South Korea but the Korea Disease Control and Prevention Agency (KDCA) said there is ***no*** direct link to the innoculations and does ***not*** plan to suspend flu shots.

2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
tba	**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*
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 4	Another in a series of sessions for industry on **Covid-19 test development**	FDA virtual Town Hall
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 12	Grand Rounds: **Facial coverings** during the Covid-19 pandemic – How well do they flatten the curve?	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 16	**Orange Book discussion**	FDA webcast
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 **To have online access, you must register by November 5**
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
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 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
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