TRENDS-in-MEDICINE

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by Lynne Peterson

Quick Takes

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

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NOTE: Subscribe to ***Trends-in-Medicine*** for coverage of the **Society of Thoracic Surgeons** (STS) meeting in New Orleans. We've added a weekly coronavirus update section (starting on Page 5).

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

✓ ABBOTT's Tendyne is the first transcatheter mitral valve replacement (TMVR) to be granted a CE Mark.

✓ AIMMUNE THERAPEUTICS' Palforzia (AR-101) was approved to treat peanut allergy.

✓ The Chinese **coronavirus outbreak** continues to expand, with >17,000 infected in China, and a growing number of countries worldwide reporting sporadic cases caused by travelers from China. This has led to travel bans, quarantines, and increasing disruption of trade and business with China. An increasing number of companies are working on either diagnostics or vaccines.

✓ **Positive trial data:**

- ACCELERON PHARMA's sotatercept in a Phase II trial in pulmonary arterial hypertension (PAH).
- ASTRAZENECA's Brilinta (ticagrelor) in a Phase III trial in stroke/TIA patients.
- ASTRAZENECA and DAIICHI SANKYO's Enhertu (trastuzumab deruxtecan) in a Phase II trial in HER2+ unresectable/metastatic gastric or esophageal junction cancer.
- BAYER and ORION's Nubeqa (darolutamide) in a Phase III trial in non-metastatic castration-resistant prostate cancer.
- EDWARDS LIFESCIENCES' Sapien XT in 5-year PARTNER-2 trial results with this TAVR.
- INCYTE's Jakafi (ruxolitinib) in a Phase III trial in atopic dermatitis.
- INCYTE and LILLY's Olumiant (baricitinib) in a Phase III trial in atopic dermatitis.
- SANOFI's olipudase alfa in a Phase II/III trial in Niemann-Pick disease.

✓ **The negative news** – Development was halted for:

- LILLY's pegilodecakin, an IL-10 receptor agonist, in NSCLC and other cancers.
- ROCHE's RG-6004, an antisense for HBV.
- SPRING BANK PHARMACEUTICALS' inarigivir soproxil (GS-9992) for HBV.
- VERTEX PHARMACEUTICALS' VX-961 for pain.

SHORT TAKES

- ACCELERON PHARMA's sotatercept, a TGF-β ligand trap, met the primary endpoint in the Phase II PULSAR trial in pulmonary arterial hypertension (PAH), significantly reducing pulmonary vascular resistance (PVR) at Week 24 vs. placebo.

- ALKERMES' ALKS-3831 (olanzapine + samidorphan) – The FDA accepted the new drug application (NDA) for this once-daily atypical antipsychotic (with less weight gain than olanzapine alone) as a treatment for *both* bipolar I disorder and schizophrenia. The PDUFA date is November 15, 2020.

- ALLERGAN is selling 3 drugs to clear the way with the U.S. Federal Trade Commission for its merger with AbbVie: brazikumab, an investigational anti-IL-23 for Crohn's disease and ulcerative colitis, to **AstraZeneca**; Zenpep (pancrelipase) for pancreatic insufficiency in cystic fibrosis patients, and Viokace, a pancreatic enzyme replacement drug, to **Nestlé**.

- AMPHASTAR PHARMACEUTICALS' epinephrine 30mg/30mL – The FDA rejected the abbreviated new drug application (ANDA) for this vasoconstrictor, issuing a complete response letter, which the company characterized as a "minor" CRL. Three days after getting the CRL, the company responded and now expects an FDA decision within 3 months. (*That is the first time we know of anyone calling a CRL "minor."*)

- APREA THERAPEUTICS' APR-246 was granted breakthrough therapy status by the FDA for use in combination with azacitidine to treat myelodysplastic syndromes (MDS) patients with a TP53 mutation.

- AVACTA's AVA04-VbP, a TMAC drug conjugate, outperformed Pfizer and Merck KGaA's Bavencio (avelumab), a PD-L1 inhibitor, in a proof-of-concept preclinical animal cancer study.

- BAYER and ORION's Nubeqa (darolutamide) – In the Phase III ARAMIS trial in non-metastatic castration-resistant prostate cancer, this oral androgen receptor inhibitor in combination with androgen deprivation therapy (ADT) significantly improved overall survival vs. ADT alone. It was previously reported that ARAMIS met the primary endpoint (metastasis-free survival).

- BIODESIX is collaborating with **Streck** to help each other get their products/services approved by the FDA – Streck's blood collection tubes and Biodesix's diagnostic testing services.

- CABALETTA BIO's DSG3-CAART, an investigational therapy for pemphigus vulgaris, was granted orphan drug status by the FDA.

- CAR T – University of Pennsylvania researchers reported in the journal ***Cancer Discovery*** that the existing CAR-T therapies – Novartis' Kymriah (tisagenlecleucel) and Gilead Sciences' Yescarta (axicabtagene ciloleucel) – which don't work in up to 20% of patients with B cell malignancies is due to the cancer, not a failure of the patient's immune system. The cancer cells may lose CD19, which is how CAR T works, the patient may have dysfunctional T cells, or there may be CD19 cells that just don't die as they should.

- Case Western Reserve University's Myeliviz, a new myelin-binding PET tracer that university researchers developed, was given the go-ahead by the FDA for clinical trials as a diagnostic for multiple sclerosis and other myelin-associated diseases.

- CELULARITY's CYNK-001 – The FDA approved an investigational new drug (IND) application for this natural killer cell therapy, clearing the way for a first-in-human trial in relapsed glioblastoma multiforme.

- CIVICA RX and **Blue Cross/Blue Shield of Vermont** are partnering on a plan to lower non-hospital generic drug prices in Vermont.

- CONATUS PHARMACEUTICALS is doing a reverse merger with **Histogen** and will take the Histogen name.

- EDWARDS LIFESCIENCES' Sapien XT – The 5-year results of the PARTNER-2 trial of this transcatheter aortic valve replacement (TAVR), published in the ***New England Journal of Medicine***, showed no significant difference in death or disabling stroke vs. surgical aortic valve replacement (SAVR), but Sapien patients had more mild paravalvular leak (PVL), more rehospitalizations, and more reinterventions vs. SAVR patients.

- EVALI update – The CDC reported that as of January 21, 2020, there were **60 confirmed deaths** from e-cigarette and vaping-associated illness (EVALI) in 27 states and the District of Columbia, with 2,711 people hospitalized for EVALI across all 50 states.

- FULCRUM THERAPEUTICS' losmapimod, a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor, was granted orphan drug status by the FDA as a treatment for facioscapulohumeral muscular dystrophy (FSHD).

- GENUS LIFESCIENCES sued the FDA, accusing the Agency of unlawfully approving **Lannett's Numbrino** (cocaine HCl) in 2020, a competitor to Genus' Goprelto (cocaine HCl nasal solution), because Goprelto was supposed to have exclusivity until 2022.

- GLAXOSMITHKLINE's M72/ASO1$_E$, an investigational tuberculosis (TB) vaccine, was licensed to the Bill & Melinda Gates Medical Research Institute, which will take over development.

- HG, a U.K.-based private equity firm, is buying **Novacap's Intelerad Medical Systems**, a medtech software firm.

- LUMIBIRD announced it is buying the laser and ultrasound business of **Ellex Medical Lasers**. (*This was first announced in December 2019, but we didn't report it at the time, and we didn't want you to miss it.*)

- Lung cancer – The results of the NELSON trial, confirming the benefits of CT lung cancer screening, were published in the ***New England Journal of Medicine***.

- MEDTRONIC's PulseSelect, a pulsed-field ablation system for treating atrial fibrillation, was granted an investigational device exemption (IDE) by the FDA, clearing the way for a non-randomized, unblinded, worldwide trial.

- REGENERON PHARMACEUTICALS and SANOFI's Dupixent (dupilumab) – The FDA accepted for priority review a supplemental biological license application (sBLA) for this anti-IL-4/13 as an add-on maintenance treatment for children age 6-11 with moderate-to-severe atopic dermatitis (AD) not adequately controlled with a topical therapy. The PDUFA date is May 26, 2020.

- SANOFI's olipudase alfa met the co-primary endpoints in a 36-patient, 12-month Phase II/III trial in Niemann-Pick disease (acid sphingomyelinase deficiency, ASMD), significantly improving lung function vs. placebo (+22% vs. +3%) and decreasing spleen volume (-39.5% vs. +0.5%).

- SEED Co., a contact lens maker, bought a 90% stake in **Sensimed**. (*This occurred in December 2019, but we did not report it at the time and didn't want you to miss it.*)

- SOLITON's Rapid Acoustic Pulse (RAP) Device – The company reported that a proof-of-concept (POC) 12-week study significantly improved the appearance of fibrotic (keloid and hypertrophic) scars, with good safety and tolerability.

- SPRING BANK PHARMACEUTICALS' inarigivir soproxil (GS-9992) – Development of this dinucleotide for hepatitis B virus (HBV) was discontinued after several serious adverse events, including a death, in the Phase IIb CATALYST trial.

Very early research news

- Oncology – Scientists at the Broad Institute and Dana-Farber Cancer Institute screened thousands of existing drug compounds and unexpectedly found ~50 they believe could be repurposed for treating cancer. They also identified novel targets that could aid in the development of new cancer drugs.

NEWS IN BRIEF

ASTRAZENECA

- **Brilinta (ticagrelor).** This blood thinner met the primary endpoint in the >11,000-patient Phase III THALES trial, with a significantly lower rate of repeat stroke or death in combination with aspirin than aspirin alone in patients with a first stroke or transient ischemic attack.

- **and DAIICHI SANKYO's Enhertu (trastuzumab deruxtecan).** This antibody-drug conjugate met the primary endpoint in the Phase II DESTINY-Gastric-1 trial in ≥3-line HER2+ unresectable/metastatic gastric cancer or gastroesophageal junction cancer, with a significant objective response rate as well as a significant and clinically meaningful improvement in overall survival.

- Is selling the global rights (except for Japan, India, and the U.S.) to five hypertension drugs to **Atnahs Pharma** – Inderal (propranolol), Tenormin (atenolol), Tenoretic (atenolol + chlorthalidone fixed-dose combination), Zestril (lisinopril), and Zestoretic (lisinopril + hydrochlorothiazide fixed-dose combination).

INCYTE

- **Jakafi (ruxolitinib).** In top-line data from the Phase III TRuE-AD2 trial, a topical form of this JAK inhibitor met the primary endpoint, with significantly more atopic dermatitis patients achieving IGA 0/1 vs. placebo, with ruxolitinib patients also having a ≥2-point improvement from baseline at Week 8.

- **and LILLY's Olumiant (baricitinib).** In top-line results from the 16-week, 463-patient Phase III BREEZE-AD4 trial in moderate-to-severe atopic dermatitis, this topical JAK inhibitor met the primary endpoint, with significantly more baricitinib patients on the 4 mg dose achieving EASI-75 vs. placebo (31.5% vs. 17.2%). Baricitinib also met the key secondary endpoints.

LILLY

- Ended development of **pegilodecakin** (AM-0010, an IL-10 receptor agonist), as well as an IDO1 inhibitor, a TIM-3 antibody, and galunisertib (a TGF-β inhibitor).
- **Reyvow (lasmiditan).** The Drug Enforcement Administration (DEA) classified this 5-HT_{1F} receptor agonist (a ditan) for acute treatment of migraine (with or without aura) a Schedule V drug, clearing the way for marketing, and Lilly set the price at $640 for 8 tablets ($80 per pill).
- **Selpercatinib (LOXO-292).** The new drug application for this RET inhibitor was granted priority review for the treatment of advanced RET fusion-positive non-small cell lung cancer (NSCLC) or thyroid cancer as well as RET-mutant medullary thyroid cancer. The exact PDUFA date was not released, but it is in 3Q20.

NOVARTIS

- **Asciminib (ABL-001).** The company said it is continuing the Phase II ASC4MORE trial of this allosteric BCR-ABL inhibitor, but the trial will no longer be used to support an FDA submission in second-line treatment of chronic myelogenous leukemia (CML).
- **Ilaris (canakinumab).** The company dropped plans for a Phase III trial of this anti-IL-1β in hereditary periodic fevers.
- Is giving up on a generic version of GlaxoSmithKline's Advair (fluticasone + salmeterol).
- **Zolgensma (onasemnogene abeparvovec-xioi).** There has been a surprisingly large number of patients (~200) who got this gene therapy for spinal muscular atrophy (SMA) in 2019, despite the $2.1 million per patient cost, and Novartis expects to treat ~100 patients each quarter this year.

Paclitaxel

Several studies were presented at the Leipzig Interventional Course (LINC) meeting in Leipzig, Germany, on paclitaxel eluting devices, including:

- **PHILIPS' Stellarex.** Four-year data from the ILLUMENATE trial showed that this low-dose drug-coated balloon had a mortality rate similar to standard of care.
- **BECTON DICKINSON/C.R. BARD's Lutonix.** An independent analysis by Syntactx, a clinical research organization (CRO), of the data on this drug-coated balloon (DCB) showed "no plausible link" between paclitaxel and mortality.
- The results of the 414-patient COMPARE trial – a head-to-head comparison of **Boston Scientific's Ranger** DCB and **Medtronic's IN.PACT Admiral** or **Pacific** DCB – presented at LINQ and simultaneously published in the ***European Heart Journal***, showed non-inferiority between the low-dose Ranger and the high-dose Admiral.

PFIZER

The company terminated a number of Phase I and II programs, including:

- Bavencio (avelumab, an anti-PD-L1) + PF-04518600 (an OX40 agonist) + utomilumab (PF-05082566, an anti-4-1BB/CD137) – a triplet for cancer. Other combination Bavencio trial plans were also dropped.
- Inlyta (axitinib) + Merck's Keytruda (pembrolizumab) – an anti-VEGFR/PD-1 combination for cancer.
- PF-06688992 in cancer.
- PF-04447943 in sickle cell disease.

ROCHE

- **RG-6004.** Development of this antisense oligonucleotide for HBV was stopped.
- **Rituxan (rituximab).** The 989-patient, 3.9-year, real-world SUNSTONE trial, published in ***Arthritis Care & Research***, found a higher risk of clinically significant infections with long-term use of this anti-CD20 in rheumatoid arthritis vs. the general population, but the rate was lower than in a similar cohort of Medicare patients.
- **Tecentriq (atezolizumab).** The company completed submission of a supplemental biologics license application (sBLA) to the FDA for use of this PD-L1 inhibitor in combination with Avastin (bevacizumab) in unresectable hepatocellular carcinoma (HCC). It is being reviewed under the real-time oncology review (RTOR) pilot program, so there isn't a specific PDUFA date.

VERTEX PHARMACEUTICALS

- **Trikafta (elexacaftor + ivacaftor + tezacaftor).** Sales in 4Q19 of this triplet treatment for cystic fibrosis were 5-times more than analysts predicted.
- **VX-961.** Development of this NaV1.8 inhibitor for acute, chronic, and neuropathic pain was halted because the company didn't like the Phase I pharmacokinetic and tolerability data.

CORONAVIRUS (2019-NCOV) UPDATE

- **Treatment.** **ABBVIE's Kaletra/Aluvia (lopinavir + ritonavir)** – The company donated ~$1.5 million worth of this protease inhibitor normally used to treat HIV to China for use in treating coronavirus patients.

- **Vaccines.** Previously we reported that Gilead Sciences, Inovio Pharmaceuticals, Moderna, Novavax, and Vir Biotechnology are working on vaccines for the coronavirus. The latest entries into the development race are:

  - **China**'s Center for Disease Control and Prevention is working on development of a vaccine.

  - **CUREVAC** is collaborating with the Coalition for Epidemic Preparedness Innovations (CEPI) on a vaccine.

  - **JOHNSON & JOHNSON**, which is working on a vaccine, though a J&J official said the company is starting from scratch and that could mean it will be up to a year before the vaccine is available for patients.

  - **Pasteur Institute Foundation** in France hopes to have a vaccine available by 2021.

  - **VAXART** initiated a coronavirus program based on its proprietary oral vaccine platform, VAAST.

- **Diagnostics.** The RT-PCR test that the CDC has been using may not be as accurate or reliable as the CDC hoped, which may explain (1) why it is taking so long to test the suspicious cases and (2) why it hasn't been rolled out to state and local health departments.

  - **ARES GENETICS and BGI GROUP** are partnering on development of molecular diagnostic tests for 2019-nCoV for use in public hospitals and health institutions in Europe. Ares plans to introduce a next-generation sequencing (NGS) testing service in February 2020 that uses a platform from BGI/MGI.

  - **ROCHE** said it has developed the first commercial test for 2019-nCoV.

  - **SANSURE BIOTECH**'s 30-minute diagnostic kits were approved in China.

- **Active pharmaceutical ingredients.** A survey by Kemiex of 97 professional buyers, traders, and producers found that 36% believe the virus will have a high impact on supply in 1Q20, with 13% expecting no impact at all.

- **Extent of the problem.**

  - The U.S. now has 11 confirmed cases of coronavirus – one in Seattle, 2 in Chicago, one in Massachusetts, one in Arizona, and 6 in California. All but two (both spouses of people with the virus who got it by person-to-person transmission) had returned from Wuhan, China. The latest cases are 3 more people in California, a young Boston, MA, man who is reported to be isolated, and a Santa Clara, CA, man who had "self-isolated" since his return from China. The Santa Clara man was ***not*** hospitalized and reportedly has come into contact with "very few" people, and those people are "self-isolating" at home for 14 days.

    (*Remember how well the self-quarantine worked during the Ebola outbreak in 2014 when NBC correspondent Nancy Snyderman and her crew were supposed to be self-isolated in New Jersey after returning from Africa – but were caught getting takeout food from a restaurant?*)

  - The number of cases of 2019-nCoV is now higher than in the whole SARS outbreak, which was 5,327 confirmed cases.

  - The death rate in China from the virus appears, for the first time, to have dipped below 3%, now standing at just over 2% (361 out of 17,205 cases according to Chinese authorities). However, a scientific model, published in ***The Lancet***, estimates the real number of cases at >75,800, with a doubling every 6.4 days.

  - The first death outside of China was reported in the Philippines. So, with 134 known cases in 28 countries, the death rate outside of China is <1%, well below the rate in China.

  - The World Health Organization finally decided to declare the coronavirus outbreak a global health emergency.

- **Transmission.** The first human-to-human transmission in the U.S. has occurred. The husband of the Chicago woman with the virus is now infected himself. Several cases of an *asymptomatic* Chinese businesswoman infecting two German colleagues in Germany – and one of those German businessmen infecting other colleagues – were reported in the ***New England Journal of Medicine***.

- **Travel.** The U.S. State Department raised its travel advisory to Level 4, which means "do not travel to China," and that Americans in China should consider departing using commercial means. Several airlines worldwide have halted or plan to halt flights into and out of China, and a few countries are banning entry to Chinese citizens. The U.S. is barring foreign nationals who have been in China in the previous 14 days and will quarantine for 14 days any Americans returning from China.

- **U.S. government efforts:**
  - President Trump created a task force to lead the U.S. response to coronavirus, headed by HHS Secretary Alex Azar.
  - FDA Commissioner Stephen Hahn, MD, announced steps the FDA is taking to help diagnostic tests obtain emergency use authorization (EUA) and the Agency's efforts to facilitate development of investigational treatments.

REGULATORY NEWS

Regulatory tidbits

- Advertising. The FDA proposed two studies to look at the impact of advertising influencers – celebrities, physicians, patients, and online Instagram influencers – who endorse drugs and other healthcare products.
- Arthroscopy. The FDA issued draft guidance on 510(k) submissions for Class II arthroscopy pump tubing sets classified under product code HRX.
- Biomarkers. The FDA issued a final guidance on the use of minimal residual disease (MRD) as a biomarker in clinical trials for certain hematologic malignancies.
- FDA guidances. The FDA's Center for Drug Evaluation and Research (CDER) released a list of the guidances it plans to issue this year.
- Fentanyl. The House voted 320-88 to approve legislation – and send it to President Trump for signature – that would allow the DEA to extend a ban on all fentanyl analogues for another 15 months while the Government Accountability Office examines the policy's impact on research.
- Gene sequencing. The Centers for Medicare and Medicaid Services (CMS) said that Medicare will cover NGS tests for patients with inherited forms of ovarian or breast cancer.
- Gene therapy. The FDA released six final guidance documents on gene therapy development which cover rare disease treatments, hemophilia, retinal disorders, investigational new drug applications, long-term follow-up, and testing of retroviral vector-based therapies.
- HIV. The FDA launched a new database for antiretroviral HIV drugs available through the President's Emergency Plan for AIDS Relief.
- Real-world data. FDA Commissioner Stephen Hahn, MD, speaking to FDA staff, emphasized the importance of patient-level data and real-world evidence (RWE). (*So, if you were concerned that Dr. Hahn would back away from RWE, he didn't.*)
- Stem cells. A California federal judge refused to grant the FDA a summary judgment that would have shut down unauthorized stem cell clinics in that state, sending the issue of FDA oversight to trial.

FDA approvals/clearances

- ABBOTT's Infinity, a directional deep brain stimulation system, was granted expanded approval to treat the symptoms of Parkinson's disease.
- AIMMUNE THERAPEUTICS' Palforzia (AR-101), an oral peanut-protein immunotherapy, was approved to reduce the incidence of allergic reactions and the severity of reactions in patients age 4-17.
- BIOINTELLISENSE's BioSticker, a single-use, on-body sensor for scalable remote care monitoring of heart rate, respiratory rate, and skin temperature at home, was cleared for use.
- BLINKTBI's EyeStat was cleared for use to measure blink reflex, and it will now be tested to see if it can aid in the early detection of the onset of neurological disorders, including multiple sclerosis.
- BOEHRINGER INGELHEIM and LILLY's Trijardy XR (empagliflozin + linagliptin + metformin) – This long-acting triple combination of an SGLT2 inhibitor + a DPP-4 inhibitor + metformin was approved to treat Type 2 diabetes.
- EKO's suite of algorithms, which combine with the company's digital stethoscopes to screen for heart conditions during routine physical exams, were cleared for use.
- GT MEDICAL TECHNOLOGIES' GammaTile was granted expanded clearance for use in treating newly-diagnosed malignant brain tumors.
- INTACT VASCULAR's Tack Endovascular System – A larger version of this dissection repair device was granted premarket approval for use in treating proximal popliteal and superficial femoral arteries with a diameter of 4-8 mm after a peripheral arterial dissection treatment during a balloon angioplasty.
- MAUNA KEA's Cellvizio 100, an endomicroscopy system for blood flow visualization with fluorescein, was granted 510(k) clearance.
- MERCK MSD's Dificid (fidaxomicin) – A new oral suspension formulation was approved to treat *Clostridioides difficile*-associated diarrhea in children age ≥6 months.
- PHARMACOSMOS THERAPEUTICS' Monoferric (injectable ferric derisomaltose) was approved to treat adults with iron deficiency anemia who fail on oral iron and patients with non-hemodialysis-dependent chronic kidney disease (CKD).

- TEVA's Ajovy (fremanezumab-vfrm) – An autoinjector for this CGRP inhibitor for migraine was cleared for use.

FDA recalls/warnings

- AUROBINDO received a new letter from the FDA warning that "official action" (sanctions) by the Agency is recommended for its solids formulation manufacturing plant in India.
- CARDINAL HEALTH recalled 9 million surgical gowns because its Chinese supplier, **Siyang HolyMed**, outsourced some of the production to a facility that was not FDA-approved. Cardinal is also recalling 2.9 million procedure kits that contain gowns sourced from Siyang HolyMed.
- Clozapine – The FDA issued a stronger safety alert that all clozapine products (Clozaril, Fazaclo ODT, and Versacloz) may cause severe constipation, leading to serious bowel problems, even death if not diagnosed and treated promptly.
- DRÄGER MEDICAL's Infinity M540 – The company received a warning letter for failure to submit a 510(k) application for this acute care system after modifying the device.

European Regulatory News

- **U.K.** – The Medicines and Healthcare products Regulatory Agency (MHRA) updated, again, its guidance on submitting clinical data for CE Mark approval of medical devices.
- ABBOTT's Tendyne, a transcatheter mitral valve replacement (TMVR), was granted a CE Mark.
- ABBVIE's Venclyxto (venetoclax) – The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) recommended approval of this Bcl-2 inhibitor in combination with Roche's Gazyvaro (obinutuzumab, Gazyva in the U.S.) to treat patients with untreated chronic lymphocytic leukemia (CLL).
- ALNYLAM's Givlaari (givosiran) – CHMP recommended approval to treat acute hepatic porphyria.
- BAYER's Nubeqa (darolutamide) – CHMP recommended approval of this oral androgen receptor inhibitor to treat prostate cancer.
- BIOFRONTERA's Ameluz (5-aminolevulinic acid HCl) – CHMP recommended expanded approval to include mild-to-moderate actinic keratoses on the extremities.
- BOSTON SCIENTIFIC's Exalt Model D, a single-use duodenoscope, was granted a CE Mark for use in endoscopic retrograde cholangiopancreatography procedures.
- BRISTOL-MYERS SQUIBB/CELGENE's Idhifa (enasidenib) – The marketing application to the EMA for this IDH2 inhibitor for treatment of acute myeloid leukemia (AML) was withdrawn because CHMP determined there was insufficient efficacy data.
- CYTOSORBENTS' CytoSorb, a device for use during cardiopulmonary bypass to remove ticagrelor (AstraZeneca's Brilique, Brilinta in the U.S.), an antiplatelet drug, from blood, was granted a CE Mark.
- EMERGENT's Vaxchora – CHMP recommended approval of this cholera vaccine.
- ESPERION THERAPEUTICS' Nilemdo (bempedoic acid), an oral, once-daily ATP citrate lyase inhibitor, and Nustendi (bempedoic acid + ezetimibe) – CHMP recommended approval of the applications (filed by FGK Representative Service) to treat adults with primary hypercholesterolemia (heterozygous familial and non-familial) or mixed dyslipidemia.
- GALAPAGOS' GLPG-1690, an investigational systemic sclerosis therapy, was granted orphan drug status.
- IMRICOR MEDICAL's Vision-MR ablation catheter was granted a CE Mark.
- LILLY's Liumjev (insulin lispro) – CHMP recommended approval to treat diabetes.
- MERCK MSD's Keytruda (pembrolizumab) – Merck withdrew its application for an expanded indication for this PD-1 inhibitor for use in treating esophageal cancer.
- NOVO NORDISK's Rybelsus (oral semaglutide) – CHMP recommended approval of this *oral* GLP-1 agonist to treat Type 2 diabetes.
- PFIZER
  - Ruxience (rituximab) – a biosimilar of Roche's Rituxan – CHMP recommended approval to treat non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, granulomatosis with polyangiitis and microscopic polyangiitis, and pemphigus vulgaris.
  - Staquis (crisaborole) – CHMP recommended approval of this topical PDE-4 inhibitor to treat atopic dermatitis.
- POLYGANICS' Liqoseal, a dural sealant patch, was granted a CE Mark for lessening cerebrospinal fluid leakage following elective cranial surgery.
- PROFUSA's Lumee, a wireless, injectable oxygen biosensor, was granted a CE Mark.

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

- BIOGEN's Plegridy (peginterferon beta-1a) – NICE recommended use for relapsing-remitting multiple sclerosis (MS).
- JOHNSON & JOHNSON's Spravato (esketamine) – NICE rejected this nasal spray treatment for treatment-resistant depression, citing both concerns about efficacy and cost-effectiveness.
- Multiple sclerosis – NICE is looking for people – both healthcare professionals (nurse, occupational therapist, pharmacist, neurologist, etc.) and lay people – to serve on a committee to update the NICE Clinical Guidelines for multiple sclerosis management.

Regulatory news from other countries

- ***China.***
  - ABBVIE's Kaletra/Aluvia (lopinavir + ritonavir) was repurposed by the National Health Commission to treat coronavirus, and AbbVie donated ~$1.5 million of the drug.
  - Coronavirus – The National Medical Products Administration (NMPA) approved four products for coronavirus detection, including reagent test kits and a sequencing system. (*Also see Page 5 of **Quick Takes***)
  - SANSURE BIOTECH's 30-minute 2019-nCoV test was approved by the NMPA and received a medical device registration certificate.
  - TILT BIOTHERAPEUTICS' TILT-123 – The development and commercialization rights to this oncolytic virus were licensed to **Biotheus**.

2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
February 3	How the public perceives and values pharmaceutical quality	FDA public meeting
February 4	Testing methods for **asbestos in talc** and cosmetic products containing talc	FDA public meeting
February 5	Oncology Center of Excellence – **product development for 2025**	FDA public workshop
February 5	Major e-cigarette manufacturers (Fontem, Juul, Logic, NJOY, and Reynolds American) will testify about the youth vaping epidemic	House Energy and Commerce Oversight and Investigations Subcommittee
February 13	Examination of under-representation of African Americans in multiple myeloma clinical trials	FDA and AACR joint workshop
February 14	**Blueprint Medicines' Ayvakit** (avapritinib, BLU-285) for *fourth-line* GIST	PDUFA date *Possible 3-month delay due to new data submission*
February 16	**Agile Therapeutics' Twirla** (AG200-15, 120 μg levonorgestrel + 30 μg ethinyl estradiol), a contraceptive patch	PDUFA date *Extended by the FDA from November 16, 2019*
February 18	**Merck MSD's Keytruda** (pembrolizumab) – 6 sBLAs for a 30-minute Q6W infusion to treat melanoma, Hodgkin's lymphoma, primary mediastinal large B-cell lymphoma, gastric cancer, hepatocellular carcinoma, and Merkel cell carcinoma	PDUFA date
February 19	**Adverse event reporting** using ICH standards	FDA public meeting
February 21	**Alder BioPharmaceuticals' eptinezumab** (ALD-403), a CGRP inhibitor for migraine	PDUFA date
February 21	**Esperion Therapeutics' bempedoic acid** monotherapy to treat hypercholesterolemia	PDUFA date
February 24	**FDA Rare Disease Day:** Supporting the future of rare disease product development	FDA public meeting
Feb. 25-26	Discussion of the evolving role of **artificial intelligence in radiological imaging**	FDA public workshop
February 26	AM: **STEBA Biotech's padeliporfin di-potassium** powder for solution for injection for treating localized prostate cancer PM: **Lilly's Cyramza** (ramucirumab) – expanded approval for use with erlotinib as a first-line treatment of metastatic NSCLC with EGFR exon 19 deletions or exon 21 substitution mutations	FDA's Oncologic Drugs Advisory Committee
February 26	**Acacia Pharma's Barhemsys** (IV amisulpride) for post-operative nausea and vomiting (PONV)	PDUFA date
February 26	**Esperion Therapeutics' bempedoic acid in combination with ezetimibe** to treat hypercholesterolemia	PDUFA date
February 27	**BeiGene's zanubrutinib**, a BTK inhibitor for mantle cell lymphoma	PDUFA date
February 28	Criticality of **tobacco use assessment** in oncology therapeutic trials	FDA-AACR-IASLD workshop
March 3	Development of **individualized therapeutics**	FDA workshop
March 4	Selection of strains for the 2020/2021 flu vaccine	FDA's Vaccines and Related Biological Products Advisory Committee
March 5	Advancing animal models for antibacterial drug development	FDA public workshop
March 5	Medical extended reality: evaluation practices for virtual and augmented reality	FDA public workshop
March 9	**Intarcia Therapeutics' ITCA-650** (exenatide implant) for Type 2 diabetes	PDUFA date
March 10	**Bristol-Myers Squibb's Opdivo** (nivolumab) **+ Yervoy** (ipilimumab) for advanced hepatocellular carcinoma	PDUFA date
March 10	Patient-focused drug development for **stimulant use disorder**	FDA public meeting
March 15	**Astellas and Seattle Genetics' enfortumab vendotin**, an antibody-drug conjugate for treating metastatic/locally-advanced urothelial cancer	PDUFA date
March 17	**Eton Pharmaceuticals' ET-105** (reformulated lamotrigine) as adjunctive therapy for partial seizures in Lennox-Gastaut syndrome patients	PDUFA date
March 23	Identification of concepts and terminology for **multi-component biomarkers**	FDA workshop
March 25	**Bristol-Myers Squibb/Celgene's ozanimod** (RPC-1063) for relapsing multiple sclerosis	PDUFA date
March 25	**Zogenix's Fintepla** (fenfluramine, ZX-008) for Dravet syndrome	PDUFA date
March 26	**Heron Therapeutics' HTX-011** (bupivacaine + meloxicam) for postoperative pain	PDUFA date
March 26	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	PDUFA date *postponed until June 26*
March 26	**IntelGenx Technologies' Rizaport** (RHB-103) for migraine	PDUFA date

more - 2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*)		
Date	**Topic**	**Committee/Event**
March 27	**Modernizing FDA's data strategy**	FDA public meeting
March 28	**Rockwell Medical's Triferic** (ferric pyrophosphate) for anemia	PDUFA date
March 30	Patient-focused drug development for **vitiligo**	FDA public meeting
March tba	**AstraZeneca's Imfinzi** (durvalumab) + tremelimumab for small cell lung cancer	PDUFA date (*estimated late March*)
April tba	**Lilly's empagliflozin + linagliptin + metformin extended-release**, a triplet for Type 2 diabetes	PDUFA date
April tba	**Puma Biotechnology's Nerlynx** (neratinib) – expanded approval as a ≥3-line treatment for HER2+ metastatic breast cancer	PDUFA date
April 1	FDA communications about the **safety of medical devices**	FDA public meeting
April 4	**Bristol-Myers Squibb/Celgene and Acceleron Pharma's Reblozyl** (luspatercept-aamt) – expanded approval to include very low-to-intermediate risk myelodysplastic syndrome-associated anemia in patients with ring sideroblasts who require red blood cell transfusions	PDUFA date
April 22 *tentative*	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	FDA's Gastrointestinal Drugs Advisory Committee
April 25	**Sanofi's MenQuadfi**, a meningococcal vaccine	PDUFA date
April 26	**Neurocrine Biosciences' opicapone** to treat Parkinson's disease	PDUFA date
April 27	**United Therapeutics' Trevyent** (treprostinil) to treat pulmonary arterial hypertension (PAH)	PDUFA date
April 30	**Sanofi's isatuximab** for relapsed/refractory multiple myeloma	PDUFA date
May 4	**2020 generic drug** regulatory science initiatives	FDA public workshop
May 12	**Johnson & Johnson and Halozyme's Darzalex** (daratumumab) subcutaneous delivery for multiple myeloma	PDUFA date (*estimated*)
May 12-13	**Regulatory education for industry**	FDA conference
May 14	**Sunovion Pharmaceuticals' dasotraline** for moderate-to-severe binge eating disorders	PDUFA date
May 15	**Allergan's bimatoprost sustained-release** for treating glaucoma	PDUFA date (*estimated*)
May 15	**Clovis Oncology's Rubraca** (rucaparib) – expanded approval to treat advanced prostate cancer	PDUFA date
May 24	**Roche's risdiplam** (RG-7916) to treat spinal muscular atrophy	PDUFA date
May 25	**Evofem Biosciences' Amphora** (L-lactic acid + citric acid + potassium bitartrate), a hormone-free contraceptive (resubmission)	PDUFA date
May 26	**Regeneron Pharmaceuticals and Sanofi's Dupixent** (dupilumab) – expanded approval to include treatment of children age 6-11 with atopic dermatitis	PDUFA date
May 30	**Incyte's pemigatinib** for previously treated, locally-advanced/metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements	PDUFA date
June 2	**Immunomedics' sacituzumab govitecan** (IMMU-132) as a ≥3-line treatment for metastatic triple-negative breast cancer	PDUFA date
June 2	**Foamix Pharmaceuticals' FMX-103** (minocycline foam) to treat moderate-to-severe papulopustular rosacea	PDUFA date
June 11	**Viela Bio's inebilizumab** for first-line monotherapy of neuromyelitis optica spectrum disorder	PDUFA date
June 26	**Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH)	PDUFA date *extended from March 26*
July 13	**Averitas Pharma's Qutenza** (capsaicin patch) – expanded approval to treat neuropathic pain from diabetic peripheral neuropathy	PDUFA date
August 5	**DBV Technologies' Viaskin Peanut** for treating children with peanut allergy	FDA target action date
August 27	**Cassiopea's clascoterone cream 1%**, a topical androgen receptor inhibitor for acne	PDUFA date
Sept. 28-30	Global summit on regulatory science: **Emerging Techologies**	FDA summit **https://aralliance.org/gsrs/**
October 24	**Spectrum Pharmaceuticals' Rolontis** (eflapegrastim) for treating chemotherapy-induced neutropenia	PDUFA date
November 15	**Alkermes' ALKS-3831** (olanzapine + samidorphan) for bipolar I disorder and schizophrenia	PDUFA date