TRENDS-in-MEDICINE

May 3, 2020

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# 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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Remember that coronavirus news is being reported in regular separate Coronavirus Update bulletins. Thus, very little coronavirus news is included in this ***Quick Takes***, *which covers two weeks.*

Subscribe to ***Trends-in-Medicine*** for coverage of the two-day virtual meeting of the American Association for Cancer Research (AACR).

**Be careful, be safe, and be well.**

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

✓ GILEAD SCIENCES' remdesivir was granted an emergency use authorization for treating hospitalized Covid-19 patients.

✓ ICER's analysis of **Vertex Pharmaceuticals**' cystic fibrosis drugs found they are effective but too expensive, yet Trikafta (elexacaftor + tezacaftor + ivacaftor) got an A rating.

✓ **Positive trial news:**

- ASTRAZENECA and MERCK MSD's Lynparza (olaparib) in metastatic castration-resistant prostate cancer patients with a BRCA or ATM mutation.
- AVADEL PHARMACEUTICALS' FT-218 (QD sodium oxybate) for cataplexy attacks in narcolepsy.
- AXSOME THERAPEUTICS' AXS-05 in agitation in Alzheimer's disease.
- BRISTOL-MYERS SQUIBB's Opdivo (nivolumab)
  + ipilimumab in previously untreated malignant pleural mesothelioma.
  + cabozatinib in advanced/metastatic renal cell carcinoma (RCC).
- CARA THERAPEUTICS and VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA's Korsuva (difelikefalin, CR-845) in hemodialysis patients with pruritus.
- IDORSIA's daridorexant in insomnia.
- MERCK MSD's Keytruda (pembrolizumab), in combination with Eisai's Lenvima (lenvatinib) in advanced endometrial cancer.
- NOVARTIS' Afinitor (everolimus) in common benign, spontaneous kidney tumors (angiomyolipomas).
- REGENERON PHARMACEUTICALS and SANOFI's Libtayo (cemiplimab) in NSCLC.
- ROCHE's risdiplam in Type 1 spinal muscular atrophy.
- SCYNEXIS' ibrexafungerp in vaginal yeast infection.

✓ **Negative trial news:** BLUEPRINT MEDICINES' avapritinib missed the primary endpoint in the Phase III VOYAGER trial in advanced gastrointestinal stromal tumor (GIST).

## SHORT TAKES

- ALMAC DISCOVERY is collaborating with Merck MSD on research into novel small molecule inhibitors against specified deubiquitinase (DUB) targets, particularly for treating neurodegenerative diseases.

- ALPHATEC has given up on its attempt to buy EOS Imaging.

- ASKBIO bought BrainVectis, a gene therapy biotech working on treatments for neurodegenerative disorders.

- ASTELLAS bought Nanna Therapeutics, which specializes in mitochondrial research.

- ASTRAZENECA and MERCK MSD's Lynparza (olaparib) – This PARP inhibitor showed a statistically significant and clinically meaningful survival benefit over either Pfizer and Astellas' Xtandi (enzalutamide) or Johnson & Johnson's Zytiga (abiraterone) in the Phase III PROfound trial in metastatic castration-resistant prostate cancer patients with a BRCA or ATM mutation. *Lynparza had already met its preliminary endpoint, radiographic progression-free survival (PFS).*

- AVADEL PHARMACEUTICALS' FT-218 (QD sodium oxybate) – All three doses tested met all three co-primary endpoints in the pivotal Phase III REST-ON trial in narcolepsy, significantly – and clinically meaningfully – improvement on maintenance of wakefulness test (MWT), clinical global impression of improvement (CGI-I), and improvement in weekly cataplexy attacks, all vs. placebo.

- AXSOME THERAPEUTICS' AXS-05, an NMDA receptor antagonist, met the primary endpoint in the 366-patient Phase II/III ADVANCE-1 trial in agitation in Alzheimer's disease, significantly improving agitation vs. placebo.

- BIOGEN's aducanumab (BIIB-037) – The company said last fall that it planned to submit this anti-beta amyloid antibody to the FDA in early 2020 based on a reanalysis of a failed Phase III trial in Alzheimer's disease, but that date has come and gone with no filing. Biogen is now saying that it is "making good progress" toward an FDA filing, which is now planned for 3Q20.

- BLUEPRINT MEDICINES' avapritinib missed the primary endpoint in the Phase III VOYAGER trial in advanced gastrointestinal stromal tumor (GIST), failing to improve PFS vs. Bayer's Stivarga (regorafenib), and Blueprint plans to discontinue all development except in PDGFRA exon 18 mutant GIST.

- CARA THERAPEUTICS and VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA's Korsuva (difelikefalin, CR-845) – This selective kappa opioid receptor agonist met the primary endpoint in top-line data from the pivotal Phase III KALM-2 trial in hemodialysis patients with pruritus, with a significantly greater improvement in worst itching intensity (NRS) score vs. placebo (54% vs. 42%).

- CASSIOPEA's clascoterone cream 1% – The results of two 12-week Phase III trials, published in ***JAMA Dermatology***, of this topical androgen receptor inhibitor showed good efficacy in treating acne, with good safety.

- CYTOSORBENTS' CytoSorb, a blood purification technology for the removal of the blood thinner ticagrelor (AstraZeneca's Brilinta) during cardiothoracic surgery in a cardiopulmonary bypass circuit, was granted breakthrough device designation by the FDA.

- DENOVO BIOPHARMA is acquiring Tocagen's retroviral replicating vector platform (RRV). This will give Denovo Tocagen's investigational gene and drug therapies, which include Toca-511 and Toca-FC (now DB-107).

- DIAMOND PHARMA SERVICES bought PharmaCentral, a pharmacovigilance services and medical affairs business.

- ENDOSPAN's NEXUS, a stent graft system used for aortic arch repair, was granted breakthrough device designation by the FDA.

- GLAXOSMITHKLINE's dostarlimab – Updated data from the GARNET trial showed this anti-PD-1 was effective in a subset of women – those with measurable disease at baseline and at ≥6 months of follow-up – with recurrent or advanced endometrial cancer who had progressed on/after platinum-based chemotherapy, with improved objective response rate and duration of response.

- IDORSIA's daridorexant – In top-line results from a 930-patient Phase III trial, this dual orexin receptor antagonist in insomnia met the primary and key secondary endpoints, significantly improving sleep onset, sleep maintenance, subjective total sleep time, and patients' daytime performance.

- INSILICO MEDICINE is collaborating with Astellas on artificial intelligence.

- JOHNSON & JOHNSON's Darzalex Faspro (daratumumab + hyaluronidase-fihj) – The results of the pivotal Phase III COLUMBA trial of this subcutaneous anti-CD38 in multiple myeloma were published in ***The Lancet Haematology***, with a positive accompanying editorial. COLUMBA showed that Darzalex SC was non-inferior to Darzalex IV, with a trough rate of 108%, an overall response rate of 41% (vs. 37%), and PFS of 5.6 months (vs. 6.1 months). There was more

Grade 3-4 neutropenia with SC (13% vs. 8%) but fewer infusion reactions (13% vs. 34%).

- LNC THERAPEUTICS licensed the rights from the University of Valencia for a patent outlining the Christensenella gut bacteria's role in mood orders.

- MERCK MSD's Keytruda (pembrolizumab) – Data from a Phase II trial, presented in a Society of Gynecologic Oncology (SGO) webinar, showed that combining this PD-1 inhibitor with Eisai's Lenvima (lenvatinib), a VEGFR inhibitor, in advanced endometrial cancer resulted in "compelling activity…regardless of microsatellite instability status, PD-L1 status, or histology." Responses were also deep and durable.

- MOGRIFY is collaborating with **Sangamo Therapeutics**, which got an exclusive license to develop allogeneic cell therapies from Mogrify's induced pluripotent stem cells and embryonic stem cells using its zinc fingers technology.

- MYOVANT SCIENCES' relugolix – A new drug application (NDA) for this oral, once-daily GnRH receptor antagonist was submitted to the FDA as a treatment for advanced prostate cancer.

- MYRIAD GENETICS' GeneSight Psychotropic Test – A meta-analysis of 4 trials with a total of 1,556 patients, showing the clinical utility of this test in people with major depressive disorder, was published in the journal ***Pharmacogenomics***. The study found that outcomes were significantly improved when patient care was guided by the GeneSight test vs. unguided care, with overall remission improved 49%.

- REGENERON PHARMACEUTICALS and SANOFI's Libtayo (cemiplimab) – This PD-1 inhibitor met the primary endpoint in the Phase III trial in first-line locally-advanced/metastatic non-small cell lung cancer (NSCLC), significantly prolonging overall survival vs. platinum doublet chemotherapy. At the advice of the data safety monitoring committee, the trial was stopped early for efficacy.

- REMEGEN's disitamab vedotin (RC-48) – The FDA granted an investigational new drug (IND) application for this humanized anti-HER2 antibody drug conjugate (ADC) clearing the way for a Phase II trial in HER2+ metastatic/unresectable urothelial cancer (UC).

- resTORbio is merging with **Adicet Bio**, with the combined company using the Adicet Bio name.

- SCYNEXIS' ibrexafungerp, an oral broad spectrum antibiotic, met the primary endpoint in the Phase III VANISH-306 trial in vaginal yeast infection, with 63.3% of women achieving clinical cure at Day 10.

- SIGA Technologies' TPOXX (tecovirimat) – The Biomedical Advanced Research and Development Authority (BARDA) signed a contract for $101.3 million of this oral treatment for smallpox.

- TAKEDA/SHIRE's Intuniv (guanfacine extended-release) – A Japanese study, published in the ***Journal of Clinical Psychiatry***, found that adults with attention-deficit/hyperactivity disorder (ADHD) who took this selective alpha2A-adrenergic receptor agonist had greater improvements vs. placebo.

- THRIVE EARLIER DETECTION's CancerSEEK – In the DETECT-A trial of 9,911 women with no known evidence or history of cancer, at one year 96 developed cancer. Of those 96, this liquid biopsy test, which interrogates genomic mutations in circulating tumor DNA (ctDNA) as well as protein markers in plasma, identified 26 (17 at an early stage, and 12 of those early enough to be surgically removed), standard screening (e.g., mammography or colonoscopy) found another 24, and 46 were identified by other methods after the women became symptomatic.

- TTP is partnering with **ODx Innovations** to bring the ODx point-of-care system for assessing urinary tract infections (UTIs) to market.

- VALNEVA's VLA-15 – **Pfizer** is collaborating on co-development and commercialization of this Lyme disease vaccine.

- VERACYTE exclusively licensed a genomics test Yale University developed for predicting disease progression in patients with idiopathic pulmonary fibrosis (IPF) for use on Veracyte's nCounter FLEX Analysis System.

- VISCARDIA's VisOne, an implantable device for treating moderate-to-severe heart failure, was granted breakthrough device designation by the FDA.

- ZAMBON/BREATH THERAPEUTICS' liposomal cyclosporine A for inhalation (L-CsA-i), a treatment for bronchiolitis obliterans syndrome, was granted fast track status by the FDA.

## Very early research news

- Blindness – A mouse study, published in the journal ***Nature***, found that skin cells could be reprogrammed into light-sensing rod photoreceptors and transplanted into the mouse eyes, allowing blind mice to detect light. And this was done without use of stem cells.

- Cardiology – A study by researchers at the University of Texas Southwestern Medical Center, published in the journal ***Nature***, suggests that blocking calcineurin in heart attack patients might allow the cardiac muscle to regenerate.

## NEWS IN BRIEF

### BRISTOL-MYERS SQUIBB

- **CC-486 (oral azacitidine).** The FDA accepted an NDA for this hypomethylating agent as a maintenance treatment for acute myeloid leukemia (AML) and granted it priority review. The PDUFA date is September 3, 2020.
- **Opdivo (nivolumab) + Yervoy (ipilimumab).** This anti-PD-1/anti-CTLA4 combination met the primary endpoint in an interim analysis of the pivotal Phase III CheckMate-743 trial in previously untreated malignant pleural mesothelioma, significantly prolonging overall survival vs. chemotherapy with no unexpected adverse events.
- **Opdivo (nivolumab) + Exelixis and Ipsen's Cabometyx (cabozantinib).** In top-line data from the Phase III CheckMate-9ER trial, this combination of a PD-1 inhibitor and a TKI met the primary endpoint in previously untreated advanced/metastatic renal cell carcinoma (RCC), significantly improving PFS vs. Pfizer's Sutent (sunitinib). The secondary endpoints of overall survival and objective response rate were also met.

### GILEAD SCIENCES

- Sued the Centers for Disease Control and Prevention (CDC), charging the CDC with violating its partnership with Gilead by illegally acquiring patents for intellectual property leading to the development of the HIV drug Truvada (emtricitabine/tenofovir disoproxil fumarate).
- KITE PHARMA is collaborating with oNKo-innate in a 3-year deal on discovery and development of next-generation drug and engineered cell therapies focused on natural killer (NK) cells.

### NOVARTIS

- and INCYTE's Jakafi (ruxolitinib). The results of the 309-patient Phase III REACH-2 trial, published in the ***New England Journal of Medicine***, showed that this JAK inhibitor met the primary endpoint, significantly improving the objective response rate at Day 28 in graft-versus-host disease (GVHD).
- Bought Amblyotech, a digital therapeutics company working on a combination game/video approach to treating amblyopia (lazy eye).
- Afinitor (everolimus). A study headed by researchers at Fox Chase Cancer Center, published in the ***Journal of Urology***, found that this mTOR inhibitor significantly decreased tumor volume in patients with common benign, spontaneous kidney tumors (angiomyolipomas).
- Kymriah (tisagenlecleucel). This CAR T therapy was granted regenerative medicine advanced therapy (RMAT) designation by the FDA for a new indication – treatment of relapsed/refractory follicular lymphoma.
- Mayzent (siponimod). Five-year data from the Phase III EXPAND trial, published in a supplementary issue of the journal ***Neurology***, showed that patients with secondary progressive multiple sclerosis (MS) were less likely to experience disability progression if they started treatment with this S1P receptor modulator early rather than later. The data also suggested that Mayzent helps delay brain atrophy, disability progression, and cognitive decline.

### ROCHE

- Ocrevus (ocrelizumab)
  - A supplemental biologics license application (sBLA) was submitted to the FDA for a shorter infusion time – 2 hours instead of the current 3.5 hours – for this anti-CD20 to treat relapsing or primary progressive multiple sclerosis.
  - Six-year data from a post hoc analysis of Phase III open-label extension studies found that initiating treatment with this anti-CD20 early reduced the risk of needing a walking aid (EDSS≥6) by 49% in relapsing multiple sclerosis patients vs. later therapy (4.3% vs. 7.2%).
- Risdiplam (RG-7916). This oral SMN2 splicing modifier met the primary endpoint in 1-year data from Part 2 of the FIREFISH trial, showing significant improvement in motor milestones in infants (age 1-7 months) with Type 1 spinal muscular atrophy (SMA), with 29% of infants sitting without support for 5 seconds by Month 12 (on BSID-III) vs. no infants in a natural history cohort. In addition 43.9% of infants were able to hold their head upright, 31.7% were able to roll to the side, and 4.9% were able to stand with support. This confirms the results of Part 1 of FIREFISH. No new safety signals were identified. Details will be presented in an American Academy of Neurology virtual event.
- Roche stopped development of:
  - **Balovaptan (RG-7314)**, a vasopressin modulator for autism. A study in adults was stopped in 1Q20 after a pre-planned futility analysis.
  - **Idasanutlin (RG-7388)**, an MDM2 inhibitor for relapsed/refractory AML.
  - A test for **nemolizumab**, an anti-IL-31 for pruritus in dialysis patients.

### SANOFI

- **Efpeglenatide.** The company is still looking for a buyer for this Type 2 diabetes drug, a long-acting GLP-1 agonist.
- **SAR-422459.** The company is still looking for a buyer for this ABCA4 gene therapy for Stargardt eye disease.
- **SAR-440340.** The company ended work on this anti-IL-33 for atopic dermatitis that was partnered with Regeneron Pharmaceuticals.
- **SAR-442168.** In a Phase IIb trial in relapsing multiple sclerosis, this BTK inhibitor (which can cross the blood brain barrier) met both the primary and the secondary end-points, significantly reducing disease activity on MRI at Week 12.

### TAKEDA

- Is collaborating with **ProThera Biologics** on development of plasma-derived inter-alpha inhibitor proteins (IAIP).
- Is selling ~110 of its over-the-counter and prescription drugs sold in Europe – along with two manufacturing sites – to **Orifarm**.

### VERTEX PHARMACEUTICALS' Trikafta (elexacaftor + tezacaftor + ivacaftor) – the ICER analysis

The Institute for Clinical and Economic Review (ICER) issued an evidence report on this CFTR modulator in treating cystic fibrosis, along with an update of three other Vertex CFTR modulators – Kalydeco (ivacaftor), Orkambi (lumacaftor + ivacaftor), and Symdeko (ivacaftor + tezacaftor) – based on new data that became available since its May 2018 review of those three drugs. The findings included:

- The prices set by Vertex – which cost "many millions of dollars over the lifetime of an average patient" – are out of proportion to their substantial benefits.
- Trikafta earned ICER's highest "A" evidence rating, with high certainty that Trikafta provides a substantial net health benefit over standard care and over Symdeko.
- Though Trikafta has not yet been studied in patients with a heterozygous *F508del* mutation and a residual function mutation, ICER determined that using Trikafta for those patients is likely to be at least as good as Symdeko, and possibly better.
- ICER did ***not*** change its previous assessment of Symdeko, Orkambi, and Kalydeco.
- All of the drugs except Trikafta meet ICER's definition of a treatment for an ultra-rare condition, which could mean better insurance coverage for the non-Trikafta drugs.
- ICER's cost-effective price for Trikafta is $67,900-$85,500/year, which is 73% less than the current list price.

## REGULATORY NEWS

### Regulatory tidbits

- **Drug imports.** The FDA is cracking down on consumer imports of prescription drugs from Canada and other countries.
- **Drug manufacturing inspections.** Pharmas in India have asked the FDA to perform virtual facility inspections during the Covid-19 pandemic.
- **Drug prices.**
  - Twelve pharmaceutical companies received a fine (totaling $17.5 million) over the last six months for failing to provide state authorities with prior notice of drug price increases and explanations for the price increases. The biggest fine went to **Collegium Pharmaceutical**.
  - A survey of generic and biosimilar drug manufacturers by the Association for Accessible Medicines (AAM) found that travel and transport costs have increased an average of 224% (with one manufacturer reporting a 413% increase) due to Covid-19 pandemic regulations and restrictions.
- **Mergers.** Sen. Elizabeth Warren (D-MA) and Rep. Alexandria Ocasio-Cortez (D-NY) proposed a ban on large company mergers and acquisitions during the Covid-19 pandemic.
- **Tariffs.** AdvaMed wrote to the U.S. Office of the Trade Representative, asking that more tariffs be lifted on medical devices, components, and supplies coming from China for use in handling the coronavirus pandemic.

### FDA approvals/clearances

- ABBVIE and JOHNSON & JOHNSON's Imbruvica (ibrutinib) was granted expanded approval for use in combination with rituximab (Roche's Rituxan) for the treatment of previously untreated patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- ASTRAZENECA's Lokelma (sodium zirconium cyclosilicate) – The label for this potassium binder was updated to include a dosing regimen for treating hyperkalemia in patients with end-stage renal disease who are on hemodialysis.
- ASTURA MEDICAL's Sirion, a lateral lumbar interbody fusion system, was granted 510(k) clearance for use in spine surgery.

- ATLAS SPINE's HiJAK SA, a standalone adjustable cervical interbody system for use in spine surgery, was granted 510(k) clearance.
- CAGENT VASCULAR's Serranator, an angioplasty balloon catheter for use in treating peripheral artery disease, was granted 510(k) clearance.
- FRESENIUS MEDICAL CARE's multiFiltrate PRO System and multiBic/multiPlus Solutions were granted an emergency use authorization (EUA) to help address shortages of continuous renal replacement therapy (CRRT) products during the Covid-19 pandemic.
- GILEAD SCIENCES' remdesivir, a direct-acting antiviral (an RNA polymerase inhibitor), was granted an EUA – not approval – for treating ***hospitalized*** Covid-19 patients. The FDA put some specific conditions on the use of remdesivir:
  - Distribution has to be controlled by the government, with Gilead supplying remdesivir to authorized distributors or directly to a U.S. government agency, who will distribute it to hospitals and other healthcare facilities, in collaboration with state/local authorities.
  - Patients must have suspected or laboratory confirmed Covid-19.
  - Patients must have severe disease, defined as blood oxygen saturation ≤94% on room air, the need for supplemental oxygen or mechanical ventilation or extracoporeal membrane oxygenation (ECMO).
  - It must be administered in an inpatient hospital setting.
  - Use must be accompanied by a Fact Sheet for healthcare providers and another one for patients and parents/caregivers.
- GLAXOSMITHKLINE's Zejula (niraparib) was granted expanded approval for use as a maintenance treatment in adults with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy.
- IMMUNOMEDICS' Trodelvy (sacituzumab govitecan-hziy) was granted accelerated approval as a ≥3-line treatment for metastatic triple-negative breast cancer.
- JOHNSON & JOHNSON's Darzalex Faspro (daratumumab + hyaluronidase-fihj) was approved to treat relapsed/refractory multiple myeloma.
- LIFE SPINE's ARx Spinal System – The company was granted expanded 510(k) clearance for implant and instru-ment additions to this system.
- MEDTRONIC's Carpediem, a continuous hemodialysis system for infants weighing 5.5-22 pounds who have fluid overload or acute kidney failure, was cleared for use.
- MERCK MSD's Keytruda (pembrolizumab) – A new dosing regimen – 400 mg Q6W – was granted accelerated approval across all currently approved adult indications. *Remember, the current dosing is 200 mg Q3W.*
- NEUROCRINE BIOSCIENCES' Ongentys (opicapone) was approved as an add-on therapy for patients with Parkinson's disease OFF episodes.
- PAVMED's CarpX, a carpal tunnel device, was granted 510(k) clearance.
- SANOFI's MenQuadfi, a quadrivalent meningococcal vaccine, was approved.
- ROCHE's Cobas HPV test was approved for use with the Cobas 6800/8800 systems as well as the Cobas 4800 system.
- SYNAPTIVE MEDICAL's Evry, a small 0.5 Tesla MRI scanner that can be used bedside and which may appeal to emergency rooms for head scans, was cleared for use.
- THERMO FISHER SCIENTIFIC's ImmunoCAP Specific IgE Stinging Insect Allergen Components, a test of a person's sensitization to insect venom proteins.

## FDA recalls/warnings

- Aquarium chloroquine – The FDA issued warning letters to two companies which distribute chloroquine phosphate for treating disease in aquarium fish – **Fishman Chemical of North Carolina and Dr. G's Marine Aquaculture** – that, even though they have not made inappropriate claims about their products, the Agency is concerned that consumers may mistake their animal products for the human drug, which is being studied for treating Covid-19.
- B. BRAUN's ceftazidime – One lot was recalled because of stability testing issues.
- Cannabidiol – The FDA issued warning letters to three companies for illegally selling unapproved products containing cannabidiol:
  - **Biota Biosciences** for marketing injectable CBD as an alternative to opioids.
  - **Homero** (dba Natures CBD Oil Distribution of New Hampshire) for marketing CBD products as a treatment for opioid addiction.
  - **Nova Botanix** (dba CanaBD) for selling unapproved and misbranded cannabidiol products with the misleading claim that they are safe and/or effective for the prevention and treatment of Covid-19.

- Covid-19 – The FDA and the FTC sent a warning letter to Prefense for offering unapproved and misbranded hand sanitizer products with misleading claims that the products are safe and/or effective for preventing/treating Covid-19.
- Electronic cigarettes – The FDA sent warning letters to 10 companies, ordering them to stop manufacturing electronic cigarette products – including vaping liquids – with packaging similar to food products as well as toys, mobile game devices, sweatshirts, and backpacks with stealth pockets that are designed to help youths conceal vaping from their parents.
- Gastric balloons – The FDA said that two of the required postmarketing studies for liquid-filled gastric balloons used for weight loss showed that two specific risks have been identified – over-inflation (spontaneous hyperinflation) and acute pancreatitis. The FDA is warning healthcare professionals about these complications so they can be part of the risk:benefit discussion with patients.
- MERCK MSD's Singulair (montelukast) – The FDA added a boxed warning to this asthma drug about serious neuropsychiatric events.
- Silver products – A federal court in Utah entered an injunction halting the sale of various silver products promoted as treatment for Covid-19.
- TRIVIDIA HEALTH's True Metrix Air – This blood glucose meter was recalled due to an incorrect factory-set unit of measure.
- VASCULAR SOLUTIONS' Langston Dual Lumen Catheter was recalled (Class I) due to the risk of separation during use.

## European Regulatory News

- Clinical trials – The European Medicines Agency (EMA) issued guidance for sponsors of clinical trials during Covid-19, detailing how they should adjust the management of both trials and participants, with specific recommendations for protocol deviations for dealing with extraordinary situations, such as the need for isolating participants, limited access to public spaces, and the reallocation of healthcare professionals.
- Medical Device Regulation (MDR) – The European Parliament voted to postpone by one year implementation of this new regulation.
- ACCORD HEALTHCARE
  - Cabazitaxel Accord (cabazitaxel) – a hybrid of Sanofi's Jevtana – The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended approval to treat hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.
  - Fingolimod Accord (fingolimod) – a generic of Novartis' Gilenya – CHMP recommended approval for treating relapsing-remitting multiple sclerosis in patients with high disease activity.
- AMYLYX's AMX-0035 (sodium phenylbutyrate + tauroursodeoxycholic acid) – The EMA's Committee for Orphan Medicinal Products (COMP) recommended this designation as an orphan medicinal product for the treatment of amyotrophic lateral sclerosis (ALS).
- BIOCEPT's Target Selector, an EGFR mutation detection assay, was granted a CE-IVD Mark.
- BOEHRINGER INGELHEIM's Ofev (nintedanib) – This TKI was approved by the European Commission as a treatment for systemic sclerosis-associated interstitial lung disease in adults.
- BRISTOL-MYERS SQUIBB/CELGENE's Reblozyl (luspatercept) – CHMP recommended approval of this erythroid maturation agent to treat adults with transfusion-dependent anemia associated with myelodysplastic syndromes.
- CERUS ENDOVASCULAR
  - 021 Contour Neovascular System for treating saccular intracranial aneurysms was granted a CE Mark.
  - Neqstent, a coil-assisted flow diverter that is used to treat intracranial aneurysms, was granted a CE Mark.
- D&A PHARMA's Hopveus (sodium oxybate) – At the request of the company, CHMP re-examined its negative opinion on this treatment for alcohol dependence but didn't change its mind.
- GILEAD SCIENCES' remdesivir – The EMA has started an accelerated review of this direct-acting antiviral (an RNA polymerase inhibitor) as a treatment for Covid-19.
- INDIVIOR's Suboxone (buprenorphine + naloxone) – CHMP recommended approval of a new formulation (sublingual film) with four new strengths for the treatment of opioid dependence.
- JOHNSON & JOHNSON's Darzalex Faspro (daratumumab + hyaluronidase) – CHMP recommended approval of this subcutaneous formulation to treat multiple myeloma.
- NOVA BIOMEDICAL's Stat EMS Basic, an emergency care fingerstick blood test that can detect levels of hemoglobin, glucose, ketone, capillary lactate, and hematocrit and provide results within 40 seconds, was granted a CE Mark.

■ NOVARTIS

- **Enerzair Breezhaler (indacaterol + glycopyrronium + mometasone)** – CHMP recommended approval as a maintenance treatment for adults with asthma that is not well controlled.
- **Zimbus Breezhaler (indacaterol + glycopyrronium + mometasone)** – CHMP recommended approval as a maintenance treatment for adults with asthma that is not well controlled.

■ PFIZER's Daurismo (glasdegib) – CHMP recommended approval to treat acute myeloid leukemia.

■ ROCHE's Ocrevus (ocrelizumab) – The EMA accepted an application for review for a shorter infusion time – 2 hours instead of the current 3.5 hours – for this anti-CD20 to treat relapsing or primary progressive multiple sclerosis.

■ SANOFI's insulin aspart – CHMP recommended this biosimilar of Novo Nordisk's NovoLog be approved to treat diabetes.

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

■ BAYER's Vitrakvi (larotrectinib) – NICE recommended use of this tumor-agnostic cancer drug for patients with NTRK+ solid tumors, and the Cancer Drugs Fund will pay for it.

■ JOHNSON & JOHNSON's Stelara (ustekinumab) – NICE recommended use of this anti-IL-12/23 to treat moderate-to-severe ulcerative colitis in patients who failed a TNF inhibitor or cannot take a TNF inhibitor.

■ PORTOLA PHARMACEUTICALS' Ondexxya (andexanet alfa) – NICE rejected this Factor Xa reversal agent, saying there is "no direct evidence" that it is better than prothrombin complex concentrate (PCC) in survival after a major bleed.

## Regulatory news from other countries

■ *Canada.* ABBOTT's FreeStyle Libre, a continuous glucose monitor (CGM), was cleared by Health Canada for remote use by diabetics during the Covid-19 pandemic.

■ *Japan.*

- ESPERION's Nexletol (bempedoic acid) and Nexlizet (bempedoic acid and ezetimibe) – Esperion is collaborating with Otsuka Pharmaceutical on development and commercialization of these oral cholesterol lowering medications in Japan.
- GILEAD SCIENCES' remdesivir – Japanese Prime Minister Shinzo Abe said this antiviral drug is expected to get a fast track review as a treatment for Covid-19.
- JOHNSON & JOHNSON's Darzalex (daratumumab) – J&J submitted a marketing application for a subcutaneous formulation (which uses Halozyme's Enhanze delivery technology) of this anti-CD38 for multiple myeloma to the Ministry of Health, Labour, and Welfare.

| 2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*) | | |
|---|---|---|
| **Date** | **Topic** | **Committee/Event** |
| May 4 | **2020 generic drug** regulatory science initiatives | FDA public workshop – virtual |
| **May 6** | Guidance for manufacturers and developers of **Covid-19 diagnostic tests** | FDA virtual Town Hall – with downloadable slides |
| May 8 | Overview and **research update** about Tumor Vaccines and Biotechnology Branch and Cellular and Tissue Therapy Branch | FDA's Cellular, Tissue, and Gene Therapies Advisory Committee *meeting by teleconference* |
| May 14 | **Sunovion Pharmaceuticals' dasotraline** for moderate-to-severe binge eating disorders | PDUFA date |
| May 14 | **Blueprint Medicines' Ayvakit** (avapritinib, BLU-285) for *fourth-line* GIST | PDUFA date *extended by FDA from February 14* |
| May 14 | **Artificial intelligence** for regulatory science research | FDA Grand Rounds lecture (webinar) |
| May 15 | Ulcerative colitis draft report to be released | ICER *Postponed from April 15 due to Covid-19* |
| 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 21** | **Aquestive Therapeutics' APL-130277** (apomorphine sublingual film) for Parkinson's disease with motor fluctuations | PDUFA date |
| May 24 | Roche's risdiplam (RG-7916) to treat spinal muscular atrophy | PDUFA date *Extended 3 months to August 24* |
| 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 | **Menlo Therapeutics/Foamix Pharmaceuticals' FMX-103** (minocycline foam) to treat moderate-to-severe papulopustular rosacea | PDUFA date |
| **June 2** | **Ex-vivo genome editing in cell therapies** | FDA webcast (1 hour) |
| June 4 | **Merck MSD's Recarbrio** (imipenem + cilastatin + relebactam) – expanded approval to treat hospital-acquired Gram-negative bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) | PDUFA date |
| **June 4** *estimated* | **AbbVie's elagolix** for uterine fibroids | PDUFA date |
| June 9 | **Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH) | FDA's Gastrointestinal Drugs Advisory Committee *Postponed from April 22 due to Covid-19* |
| June 9 | **Refocus Group's VisAbility Micro Insert for treating presbyopia** | FDA's Ophthalmic Devices Advisory Committee |
| June 11 | **Viela Bio's inebilizumab** for first-line monotherapy of neuromyelitis optica spectrum disorder | PDUFA date |
| **June 16** | **Merck MSD's Keytruda** (pembrolizumab) for solid tumors TMB-H ≥10 mutations | PDUFA date |
| **June 18** | **Ultragenyx and Kyowa Kirin's Crysvita** (burosumab-twza) for tumor-induced osteomalacia | PDUFA date |
| June 18 | **Epizyme's Tazverik** (tazemetostat) – expanded approval to treat relapsed/ refractory follicular lymphoma | PDUFA date |
| **June 19** | **Nabriva Therapeutics' Contepo** (fosfomycin), an IV antibiotic for complicated urinary tract infections | PDUFA date |
| **June 19** | **Evoke Pharma's Gimoti** (EVK-001) for female diabetic gastroparesis | PDUFA date |
| **June 23** | **Karyopharm's Xpovio** (selinexor) for diffuse large B-cell lymphoma | PDUFA date |
| June 25 | **Zogenix's Fintepla** (fenfluramine, ZX-008) for Dravet syndrome | PDUFA date *Extended from March 25 due to company submission of new data* |
| June 26 | **Intercept Pharmaceuticals' obeticholic acid** to treat liver fibrosis due to non-alcoholic steatohepatitis (NASH) | PDUFA date *extended from March 26* |
| June 26 | **Heron Therapeutics' HTX-011** (bupivacaine + meloxicam) for postoperative pain | PDUFA date *Extended by the FDA from March 26* |
| **June 26** | **Chiasma's Mycapssa** (octreotide) for acromegaly | PDUFA date |

| more - 2020 FDA Advisory Committees and Other Regulatory Dates of Interest (*items in RED are new since last week*) | | |
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| **Date** | **Topic** | **Committee/Event** |
| June 27-July 1 | **AFDO annual educational conference** | FDA's National Center for Toxicological Research |
| June 30 | **Modernizing FDA's Data Strategy** | FDA public meeting *Originally scheduled for March 27* |
| June 30 | **Modernizing FDA's Data Strategy** | FDA public meeting *Originally scheduled for March 27* |
| July 5 | **Acacia Pharma's Byfavo** (remimazolam), an ultra-short-acting and reversible anesthetic for use in surgery and other invasive procedures | PDUFA date<br>*Extended from April 5 by FDA due to new data submission* |
| July 13 | **Averitas Pharma's Qutenza** (capsaicin patch) – expanded approval to treat neuropathic pain from diabetic peripheral neuropathy | PDUFA date |
| August 4 | Development of **antifungal drugs** to treat unmet medical need | FDA public workshop *Rescheduled from May 7* |
| August 5 | Development of **antifungal drugs to treat Valley Fever** (coccidioidomycosis) | FDA public workshop *Rescheduled from May 8* |
| August 5 | **DBV Technologies' Viaskin Peanut** for treating children with peanut allergy | FDA target action date |
| August 7 | **Trevena's Olinvo** (oliceridine) for moderate-to-severe pain in hospitalized patients | PDUFA date |
| August 10 | **Gilead Sciences/Kite Pharma's KTE-X19** for relapsed/refractory mantle cell lymphoma | PDUFA date |
| August 13 | **Deciphera Pharmaceuticals' ripretinib** (DCC-2618) for GIST | PDUFA date |
| August 17 | **Bristol-Myers Squibb/Celgene/Juno Therapeutics' lisocabtagene maraleucel** (JCAR-017, liso-cel) for DLBCL | PDUFA date |
| August 20 | **Seattle Genetics' tucatinib** – in combination with Roche's Herceptin + Xeloda – to treat breast cancer | PDUFA date |
| August 21 | **BioMarin Pharmaceutical's valoctocogene roxaparvovec**, a gene therapy for hemophilia A | PDUFA date |
| August 24 | **Roche's risdiplam** (RG-7916) to treat spinal muscular atrophy | PDUFA date *Extended from May 24* |
| August 27 | **Cassiopea's clascoterone cream 1%**, a topical androgen receptor inhibitor for acne | PDUFA date |
| August 30 | **MorphoSys and Incyte's tafasitamab** for use in combination with lenalidomide to treat relapsed/refractory diffuse large B-cell lymphoma | PDUFA date |
| **September 3** | **Bristol-Myers Squibb's CC-486** (oral azacitidine) for acute myeloid leukemia | PDUFA date |
| September 27 | **Aquestive Therapeutics' Libervant** (diazepam buccal film) for seizure clusters in epileptics | PDUFA date |
| Sept. 28-30 | Global summit on regulatory science: **Emerging Techologies** | FDA summit **https://aralliance.org/gsrs/** |
| October 18 | **Roche's Herceptin** (trastuzumab) **+ Perjeta** (pertuzumab) – a fixed dose combination to treat HER2+ breast cancer | PDUFA date |
| October 24 | **Spectrum Pharmaceuticals' Rolontis** (eflapegrastim) for treating chemotherapy-induced neutropenia | PDUFA date |
| October 25 | **Regeneron Pharmaceuticals' REGN-EB3** for Ebola | PDUFA date |
| November 15 | **Alkermes' ALKS-3831** (olanzapine + samidorphan) for bipolar I disorder and schizophrenia | PDUFA date |
| November 25 | **Revance Therapeutics' daxibotulinumtoxinA** for moderate-to-severe glabellar lines | PDUFA date |
| December tba | **Pfizer and Lilly's tanezumab** to treat moderate-to-severe osteoarthritis pain | PDUFA date |
| December 3 | **BioCryst Pharmaceuticals' berotralstat** (BCX-7353) for hereditary angioedema attacks | PDUFA date |
| December 20 | **FibroGen and AstraZeneca's roxadustat** for anemia of chronic kidney disease | PDUFA date |
| December 26 | **Sumitomo Dainippon Pharma/Urovant Sciences' vibegron** for overactive bladder | PDUFA date |
| December 30 | **Almirall and Athenex's tirbanibulin** (KX2-391, KX-01) for actinic keratosis | PDUFA date |