TRENDS-in-MEDICINE

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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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NOTE: There is no Covid-19 news in this issue of ***Quick Takes*** because we will put out a Covid-19 bulletin soon instead. Subscribe to ***Trends-in-Medicine*** for our coverage of the American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO-GI).

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

✓ There were a lot of new collaborations, partnerships, purchases, and FDA breakthrough designations this week.

✓ **Positive trial news:**

- **BioMarin Pharmaceutical's Roctavian** (valoctocogene roxaparvovec) – in hemophilia A.
- **Glaukos' iDose TR** and **iStent infinite** – in open-angle glaucoma.
- **Ipsen's Dysport** (abobotulinumtoxinA) – in a number of new analyses in neurological uses.
- **Knopp Biosciences' dexpramipexole** – in moderate-to-severe eosinophilic asthma.
- **Lilly's donanemab** – in cognition in mild-to-moderate Alzheimer's disease.
- **Roche's TNKase** (tenecteplase) – vs. alteplase in basilar artery occlusion.
- **SanBio's SB-623** – in traumatic brain injury.
- **Sanofi's Lemtrada** (alemtuzumab) – in relapsing-remitting MS.
- **Verve Therapeutics' VERVE-101** – in preclinical data in heterozygous familial hypercholesterolemia.

Short Takes

- **AbbVie** licensed the first TriNKET drug candidate, an NK cell engager-based immunotherapy, from **Dragonfly Therapeutics**.
- **AbSci** bought **Denovium**, an artificial intelligence, deep-learning company, which gives it the Denovium Engine for use in drug discovery.
- **Acorda Therapeutics' Inbrija (levodopa inhalation powder)** – The manufacturing operation for this Parkinson's disease drug is being sold to **Catalent**, with Catalent agreeing to manufacture and supply the drug to Acorda.
- **Amgen** is buying molecules which target dendritic cells to evoke immune tolerance in regulatory T cells from **Evoq Therapeutics**.

- **ATAI LIFE SCIENCES** bought a majority stake in **Recognify Life Sciences**, which is developing treatments for cognitive impairment in schizophrenia.

- **BAYER's finerenone (BAY-94-8862)** – The FDA accepted a new drug application (NDA) and granted priority review to this mineralocorticoid receptor antagonist (MRA), to treat Type 2 diabetics with chronic kidney disease (CKD). The PDUFA date is in July 2021.

- **BEIGENE's tislelizumab**, a PD-1 inhibitor, was licensed to **Novartis** for North America, Europe, and Japan.

- **BIOGEN** is collaborating with **Apple** on an observational study to identify digital biomarkers of cognitive health using Apple Watch and iPhone.

- **BIOMARIN PHARMACEUTICAL's Roctavian (valoctocogene roxaparvovec)** – Data from the 134-patient Phase III GENEr8-1 trial in hemophilia A showed that at 71.6 weeks, a single dose of this gene therapy significantly reduced the annualized bleeding rate by 84% and the mean annualized Factor VIII infusion rate by 99% – and it showed superiority to the current standard of care (FVIII prophylactic therapy). Importantly, data on the subset of patients with 2-year data showed a slower rate of decline in Factor VIII expression vs. the same patients at 1 year.

- **BLUEBIRD BIO** is spinning off its oncology business into a new company, which does not yet have a name. bluebird will focus on gene and cell therapies for beta thalassemia, cerebral adrenoleukodystrophy, and sickle cell disease.

- **BOEHRINGER INGELHEIM** is collaborating with **Google** on research and implementation of quantum computing for pharma research and development.

- **COGNITO THERAPEUTICS**' non-invasive gamma frequency neurostimulation device (a digital therapeutic) was granted breakthrough device status by the FDA as a treatment for cognitive and functional symptoms of Alzheimer's disease.

- **ELIGO BIOSCIENCE's EB-005** – GlaxoSmithKline is partnering with Eligo on this investigational treatment/preventive for acne vulgaris, a CRISPR-based therapeutic for strain-specific microbiome modulation.

- **Generic drugs** – Mark Cuban has a new company – Mark Cuban Cost Plus Drug Company – which aims to offer cheap (*the cheapest?*) generic drugs, with transparent pricing and a flat 15% margin on all wholesale products.

- **HELIUS MEDICAL TECHNOLOGIES' portable neuromodulation stimulator (PoNS)** – The company submitted its response to the FDA's request for more information about this device to treat walking difficulties in people with multiple sclerosis (MS).

- **HUTCHISON CHINA MEDITECH** (Chi-Med) is partnering with **Inmagene Biopharmaceuticals** on development of four preclinical drugs to treat immunological diseases, but Chi-Med is retaining first rights in mainland China.

- **ILLUMINA's TruSight Oncology 500 (TSO 500)** – Illumina is partnering with four companies – Bristol-Myers Squibb, Kura Oncology, Merck MSD, and Myriad Genetics – to advance comprehensive genomic profiling with this pan-cancer assay.

- **IPSEN's Dysport (abobotulinumtoxinA)** – New analyses of the pivotal Phase III trial of this toxin, presented at the TOXINS 2021 virtual meeting, found that "a large proportion" of patients did not require retreatment for at least 12 weeks (16 weeks for pediatric upper limb spasticity).

- **KNOPP BIOSCIENCES' dexpramipexole**, an oral selective eosinophil maturation inhibitor, met the primary endpoint in the dose-ranging, 12-week, 103-patient Phase II EXHALE trial in moderate-to-severe eosinophilic asthma, significantly reducing the blood absolute eosinophil count (AEC) vs. placebo.

- **LILLY's donanemab** – which targets N3pG beta amyloid – met the primary endpoint in the Phase II TRAILBLAZER-ALZ trial, significantly slowing decline in cognition and daily function on the iADRS in mild-to-moderate Alzheimer's patients at Week 76.

- **MERCK MSD's V114**, a 15-valent pneumococcal conjugate vaccine, was granted fast-track status by the FDA. The PDUFA date is July 18, 2021.

- **NEWAMSTERDAM PHARMA** got funding to take an old CETP inhibitor from **Amgen** – **obicetrapib** – and give it a new try in a Phase III trial to treat high cholesterol. (*And you thought you heard the last of CETP inhibitors!*)

- **NOVARTIS' ligelizumab (QGE-031)**, an anti-IgE, was granted breakthrough therapy designation by the FDA for treating chronic spontaneous urticaria in patients with an inadequate response to H1-antihistamine treatment.

- **PAREXEL** is collaborating with **Signify Health** to improve diversity in clinical trials.

- **PENUMBRA's Indigo Aspiration System** – A study, published in ***JACC: Cardiovascular Interventions***, found that Indigo use in pulmonary embolism procedures significantly reduced the RV/LV ratio, avoided intra-procedural thrombolytics in 98.3% of patients, and had a low major adverse event rate.

- **PRECISION MEDICINE GROUP** bought **Project Farma**, a bioengineering services firm.
- **ROCHE's TNKase (tenecteplase)** – A small retrospective study found that reperfusion was better in basilar artery occlusion with tenecteplase than Roche's Activase (alteplase).
- **ROOSTERBIO** is collaborating with **Sartorius** on gene therapy manufacturing.
- **SANBIO's SB-623** – This allogeneic-modified bone marrow-derived mesenchymal stromal/stem cell therapy met the primary endpoint in interim results of the Phase II STEMTRA trial in patients with traumatic brain injury, showing significantly better improved motor status.
- **SENSYNE HEALTH** is collaborating with **Phesi**, an artificial intelligence company, on development of synthetic control arms for clinical trials.
- **SILO PHARMA** is collaborating with the University of Maryland on research and development of a targeted therapy delivery system for multiple sclerosis using peptides.
- **STERIS** is buying **Cantel Medical**.
- **TAKEDA** is partnering with **KSQ Therapeutics** on research, development, and commercialization of new immunotherapies. Under the deal, Takeda gets exclusive worldwide rights to cell and non-cell therapies that modulate targets identified using KSQ's CRISPRomics technology.
- **TAYSHA GENE THERAPIES** and the University of Texas Southwestern Medical Center jointly launched an innovation fund for discovery and development of novel gene therapies to treat central nervous system diseases.
- **THERMO FISHER SCIENTIFIC** bought Novasep's viral vector manufacturing division, **Henogen**.
- **UROGEN PHARMA** is collaborating with MD Anderson Cancer Center on a three-year effort to advance combinatorial intravesical immunotherapy with UGN-201, a TLR7/8 agonist and UGN-301, an anti-CTLA4 – delivered directly to the bladder – to treat high-grade non-muscle invasive bladder cancer.
- **VERVE THERAPEUTICS' VERVE-101**, a one-time gene-editing treatment for heterozygous familial hypercholesterolemia, showed durable and consistent LDL lowering at 6 months in non-human primates.

Animal health news

- **ANIVIVE LIFESCIENCES' Laverdia-CA1 (verdinexor tablets)** was conditionally approved by the FDA to treat dogs with lymphoma.

Very early research news

- **Prostate cancer** – Researchers, led by experts at Case Western Reserve University, have developed an MRI platform, RadClip, that their study, published in ***EBioMedicine***, showed is more accurate in predicting the risk of recurrent prostate cancer better than scoring on the Cancer of the Prostate Risk Assessment (CAPRA) score and Decipher Biosciences' Decipher Prostate test.

NEWS IN BRIEF

Drug prices

A report by the Institute on Clinical and Economic Review (ICER) on *unsupported* price increases (UPIs) in 2019 showed that the worst offender by a long shot was Amgen's Enbrel (etanercept).

ICER List of Worst *Unsupported* Price Increases in 2019

Drug	Wholesale acquisition cost (WAC) increase	Net price increase	U.S. drug spend increase
Amgen's **Enbrel** (etanercept)	5.4%	8.9%	$403 million
Johnson & Johnson's **Invega Sustenna** (paliperidone palmitate)	6.8%	10.7%	$203 million
Bausch Health/Salix Pharmaceuticals' **Xifaxan** (rifaximin)	8.4%	13.3%	$173 million
Bristol-Myers Squibb's **Orencia** (abatacepte)	6%	7.4%	$145 million
Biogen's **Tecfidera** (dimethyl fumarate)	6%	3.7%	$118 million
AbbVie's **Humira** (adalimumab)	6.2%	2%	$66 million
Novartis' **Entresto** (sacubitril + valsartan)	9.6%	8%	$66 million
UCB's **Vimpat** (lacosamide)	7%	5.6%	$58 million
Takeda's **Entyvio** (vedolizumab)	6.4%	2.3%	$48 million
Pfizer and Astellas' **Xtandi** (enzalutamide)	5.9%	2.5%	$37 million

GILEAD SCIENCES

- **Selgantolimod.** Gilead is collaborating with **Vir Biotechnology** to test the combination of this TLR-8 agonist with Vir's VIR-2218, an siRNA, plus a marketed PD-1 inhibitor to try to achieve a cure of hepatitis B virus.
- **Kite** is partnering with **Oxford BioTherapeutics** on research into five oncology targets. Those that pan out will be developed and commercialized by Gilead/Kite.

GLAUKOS

The company reported positive results from two trials:

- **iDose TR (sustained-release travoprost implant)** substantially reduced intraocular pressure (IOP) in 24-month interim results from a 36-month, 154-patient, double-masked Phase IIb trial in open-angle glaucoma vs. topical timolol BID (-7.9 mmHg for the fast-release formulation, -7.4 mmHg for the slow-release formulation, and -7.8 mmHg for timolol). *If these results hold, it will meet the primary endpoint of non-inferiority to timolol.*
- **iStent infinite.** The 12-month results of a pivotal, single-arm, 72-patient trial of this 3-stent, wide-flange version of the iStent Inject showed substantially reduced mean diurnal IOP in open-angle glaucoma patients.

SANOFI

- Is buying Kymab, which will give it KY-1005, an OX40L for atopic dermatitis and perhaps other immune-mediated diseases and inflammatory disorders.
- Licensed the rights to **Biond Biologics' BND-22**, a preclinical checkpoint inhibitor that targets ILT2.
- **Lemtrada (alemtuzumab)** slowed the progression of relapsing-remitting multiple sclerosis to secondary progressive MS in a 6-year, 1,093-patient study, published in the ***Multiple Sclerosis Journal – Experimental, Translational, and Clinical***.

Surgical robots

In an article in ***Becker's ASC Review***, administrators of three ambulatory surgery centers (ASCs) offered their view of the viability of the robots for total joint replacements (TJRs) in ASCs.

- A New Jersey administrator said they don't have a robot, and there is no demand for one for TJRs, but they are considering a robot for general and OB-GYN laparoscopic procedures, though concerns include cost and reimbursement and setup time.
- A North Carolina administrator said a robot is important for attracting patients.
- An Illinois administrator plans to get a robot after the pandemic for use in TJRs, in part because it will help recruit new surgeons.

REGULATORY NEWS

Regulatory tidbits

- **Centers for Medicare and Medicaid Services (CMS)**
  - **Breakthrough devices.** CMS finalized a rule that will expedite the Medicare coverage process for medical devices with breakthrough status, allowing automatic coverage of FDA-approved products for up to 4 years. Beyond that will require a re-evaluation.
  - **Nephrology.** The 2021 Medicare conversion factor for nephrology will be $34.89 instead of the previously announced $32.41, which translates to an ~3.3% reduction in reimbursement in 2021 vs. a 10.2% cut. In addition, the outpatient dialysis codes were preserved.
- **Continuous glucose monitors (CGMs)** – The proposed 2021-2022 California budget includes $12 million in funding to expand Medicaid coverage of CGMs in the state.
- **FDA**
  - **Artificial intelligence (AI).** The FDA published an action plan for medical AI algorithms, including draft guidance.
  - **Bioequivalence.** The FDA published new guidance for industry on protecting participants in bioequivalence studies during the Covid-19 pandemic.
  - **Covid-19.** The FDA released potency assay guidance for manufacturers of Covid-19 monoclonal antibodies and therapeutic proteins.
  - **Paclitaxel devices.** An FDA letter, published in the ***New England Journal of Medicine***, offered the Agency's view of the results of the recently published SWEDEPAD trial results comparing paclitaxel-coated devices to uncoated devices in peripheral artery disease (PAD). The FDA's take: the new data are "reassuring" because the mortality rates appear to be similar between coated and uncoated devices, but the Agency still wants to see 5-year data.
  - **Regulatory focus.** The FDA released a report on the Agency's areas of focus in regulatory science in 2021, and those include: data use, innovation in choice and competition, and empowering consumers/patients.

- **Healthcare personnel** changes coming with the new Biden administration:
  - **FDA Commissioner** Stephen Hahn, MD, is on the way out, and the interim replacement is expected to be Janet Woodcock, MD, former director of the FDA's Center for Drug Evaluation and Research. Among the candidates for the permanent commissioner are Dr. Woodcock and Joshua Sharfstein, MD, vice dean for Public Health Practice and Community Engagement at Johns Hopkins.
  - Contrary to what you may have heard, **Health and Human Services Sec. Alex Azar** did ***not*** resign, but he will leave office when the Trump presidency ends.
  - **Operation Warp Speed** chief Moncef Slaoui, PhD, will be replaced by former FDA Commissioner David Kessler, MD.
  - The new White House science advisor will be **Eric Lander**, PhD, the founding director of the Broad Institute, and it will become a cabinet level position.

FDA approvals/clearances

- **ABBOTT** received 510(k) clearance for the first rapid hand-held traumatic brain injury (TBI) blood test, which will run on Abbott's handheld i-STAT Alinity platform.
- **AI METRICS' AI Mass**, an artificial intelligence-based oncology image-analysis platform, was granted 510(k) clearance.
- **CLEARMIND BIOMEDICAL's Axonpen**, a neuroendoscope system, was cleared for use in illumination and visualization of intracranial tissue and fluids and the aspiration of tissue and/or fluid during surgery.
- **KENT IMAGING's Snapshot$_{NIR}$ v3.0**, a non-invasive tissue oxygenation imaging system for use in surgery and wound care, was granted 510(k) clearance.
- **SPARK BIOMEDICAL's Sparrow Therapy system**, a wearable neurostimulator for treating opioid withdrawal, was granted 510(k) clearance.

FDA recalls/warnings

- **BOSTON SCIENTIFIC's Lotus Edge** – All unused inventory of this transcatheter aortic valve replacement (TAVR), which the company last year discontinued, is now being formally recalled due to problems with the delivery system.
- **Chemotherapy agents** – The FDA alerted healthcare professionals to labeling updates for the preparation of vinca alkaloids, a group of chemotherapy agents that includes vincristine sulfate injection, vinblastine sulfate (for) injection, and vinorelbine tartrate injection in an effort to reduce the potential for unintended intrathecal (spinal) administration, which can cause death or severe neurological injury.
- **FRESENIUS KABI's ketorolac tromethamine** – One lot of this non-steroidal anti-inflammatory agent was recalled due to the presence of particulates in some vials.

European Regulatory News

- **AERIE PHARMACEUTICALS' Roclanda (netarsudil + latanoprost)** was approved by the European Commission to treat elevated intraocular pressure in adults with primary open-angle glaucoma or ocular hypertension not resolved with a prostaglandin or Aerie's Rhopressa (netarsudil).
- **ROCHE's Xofluza (baloxavir marboxil)** – The European Commission approved a single-dose of this antiviral to treat uncomplicated influenza and as a post-exposure prophylaxis of influenza in people age ≥12.
- **THERAPIXEL's Mammo Screen**, an artificial intelligence-based software that helps radiologists identify suspicious mammograms and lesions, was granted a CE Mark.
- **VIIV HEALTHCARE's Tivicay (dolutegravir)** – A dispersible tablet formulation of this HIV drug was approved by the European Commission to treat children.

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

- **GLAXOSMITHKLINE's Zejula (niraparib)** – NICE recommended use of this PARP inhibitor to treat Stage ≥3 advanced high-grade epithelial ovarian, Fallopian tube, or primary peritoneal cancer, regardless of BRCA status.

2020-2021 FDA Advisory Committees and Other Regulatory Dates of Interest *RED are new since last week*)		
Date	**Topic**	**Committee/Event**
November 16	**Bristol-Myers Squibb/Celgene/Juno Therapeutics' lisocabtagene maraleucel** (JCAR-017, liso-cel) for DLBCL	PDUFA date missed. *No decision announced yet*
November 25	**Revance Therapeutics' daxibotulinumtoxinA** for glabellar lines	PDUFA date *Delayed by FDA No new date announced.*
December tba	**Pfizer and Lilly's tanezumab** to treat moderate-to-severe osteoarthritis pain	PDUFA date missed *No decision announced yet*
2021		
January 20	**Merck MSD and Bayer's vericiguat** in HFrEF	PDUFA date
January 22	**Aurinia Pharmaceuticals' voclosporin** for treating lupus nephritis	PDUFA date
January 23	**Pfizer's Xalkori** (crizotinib) – expanded approval for pediatric lymphoma	PDUFA date
January 26	Non-clinical immunogenicity assessment of **generic peptide products**	FDA virtual public workshop
January 27	Interim assessment of the **biosimilar user fee act** for FY2018-2022	FDA virtual public meeting
January 27	**Coronavirus test** development and validation (series)	FDA virtual town hall
January 27	**Protalix BioTherapeutics and Chiesi's pegunigalsidase alfa** (PRX-102) for Fabry disease	PDUFA date
January 28	**Amgen's Nplate** (romiplostim) – expanded approval to treat hematopoietic syndrome of acute radiation syndrome	PDUFA date
January 29	Regulatory perspective for development of **drugs to treat NASH**	FDA webcast
February 1	**Adamas Pharmaceuticals' Gocovri** (amantadine extended-release) – expanded approval to treat Parkinson's disease patients with OFF episodes on levodopa	PDUFA date
February 1	**Safer technologies** program final guidance	FDA webcast
February 2	Inclusion of **pregnant women** in clinical trials	FDA virtual public meeting
February 2	**Mallinckrodt's StrataGraft**, a regenerative skin tissue therapy	PDUFA date
February 2-3	Scientific and ethical considerations for **pregnant women in clinical trials**	FDA virtual public meeting
February 2-3	A research agenda on barriers and solutions to oral anti-cancer agent adherence	FDA-ASCO virtual workshop
February 9	**Merck MSD's Keytruda** (pembrolizumab) – expanded approval to treat high-risk, early-stage triple-negative breast cancer	FDA's Oncologic Drugs Advisory Committee virtual meeting
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 15	**TG Therapeutics' umbralisib** for previously treated marginal zone lymphoma	PDUFA date
February 16-17	**Evaluating real-world evidence** from observational studies	FDA and Duke-Margolis Center for Health Policy virtual workshop
February 17	**Becton Dickinson/C.R. Bard's Lutonix 014**, a drug-coated balloon to treat obstructed popliteal, tibial, and peroneal arteries	FDA's Circulatory System Devices Advisory Committee virtual meeting
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 8	Patient-focused drug development for **vitiligo**	FDA virtual public meeting
March 20	**FibroGen and AstraZeneca's roxadustat** for anemia of chronic kidney disease	PDUFA date *Extended by FDA from December 20, 2020*
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
March 30-31	**Oncology drug development**	FDA virtual workshop
May 14	**Apellis Pharmaceuticals' pegcetacoplan** for treating PNH	PDUFA date
May 18	**Sanofi's avalglucosidase alfa** for Pompe disease	PDUFA date
May 21	**ADC Therapeutics' loncastuximab tesirine** for relapsed/refractory DLBCL	PDUFA date
May 30	**Kadmon's belumosudil** for chronic graft-versus-host disease after hematopoietic stem cell transplant	PDUFA date
June 15	**TG Therapeutics' umbralisib** for previously treated follicular lymphoma	PDUFA date
June 30	**Lupin Pharmaceuticals' Solosec** (secnidazole) – expanded approval to treat trichomoniasis	PDUFA date