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…

Trends-in-Medicine
Stephen Snyder, *Publisher*
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-285-0801
Fax 772-334-0856
www.trends-in-medicine.com
TrendsInMedicine@aol.com

NOTE: There was so much Covid-19 news this week that we will again have a special bulletin on it in the next day or two. Please subscribe to ***Trends-in-Medicine*** for our coverage of the virtual AF Symposium and the virtual International Association for the Study of Lung Cancer (IASLC)'s 2020 World Conference on Lung Cancer Singapore (yes, 2020 because it was delayed from last fall. There will be a 2021 meeting this fall.)

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

✓ **BELLICUM PHARMACEUTICALS' BPX-601** – The FDA lifted its clinical hold on a Phase I/II trial of this GoCAR T in metastatic pancreatic or prostate cancer.

✓ **NOVARTIS' inclisiran** – ICER said this long-acting drug for hypercholesterolemia would need to be priced at $3,600-$6,000/year to be cost-effective.

✓ **Positive trial news:**

- **BIOINVENT's BI-1206** – in relapsed NHL.
- **MYOVANT SCIENCES and PFIZER's Orgovyx** (relugolix) – in dysmenorrhea in endometriosis.
- **REVANCE THERAPEUTICS' daxibotulinumtoxinA** – in moderate-to-severe upper facial lines.
- **RHYTHM PHARMACEUTICALS' Imcivree** (setmelanotide) – in rare genetic obesity.
- **ROCHE's faricimab** – in wet AMD.
- **VIR BIOTECHNOLOGY's VIR-3434** – in HBV.

✓ **Negative trial news:**

- **PFIZER's Xeljanz** (tofacitinib) – in a postmarketing safety trial in rheumatoid arthritis.

SHORT TAKES

■ **ALBIREO PHARMA's odevixibat (A-4250)** – The FDA accepted a new drug application (NDA) for this non-systemic ileal bile acid transport inhibitor (IBATi) and granted it fast track review as a treatment for pruritus in pediatric patients with progressive familial intrahepatic cholestasis (PFIC). The PDUFA date is July 20, 2021.

■ **ALLEVIANT MEDICAL's Left Atrial Decompression System (LADS)**, a minimally-invasive transcatheter device that is used to decompress the left atrium, was granted break-through device designation by the FDA. The device works without a permanent cardiac implant or open-heart surgery in patients with heart failure with preserved ejection fraction (HFpEF) – and in whom the ejection fraction is in the mid-range, so called HFmrEF – on optimal medical therapy.

- **ATAI LIFE SCIENCES** is collaborating with Massachusetts General Hospital on development of psychedelic and non-psychedelic compounds for a variety of mental health indications.

- **BELLICUM PHARMACEUTICALS' BPX-601** – The FDA lifted the clinical hold that had halted patient enrollment and dosing in a Phase I/II dose-escalation trial of this GoCAR T + rimiducid (AP-1903), a lipid-permeable tacrolimus analog and a protein dimerizer, in patients with previously treated metastatic pancreatic or prostate cancer. No protocol changes were imposed.

- **BIOINVENT's BI-1206** – In a Phase I study this anti-FcyRIIB antibody restored the activity of rituximab (Roche's Rituxan) in relapsed non-Hodgkin's lymphoma (NHL) patients, with 6 of 9 patients who completed the induction cycle having either a complete response (CR) or partial response (PR) – and some patients having a long-lasting response.

- **CATABASIS PHARMACEUTICALS** bought **Quellis Biosciences**, which will give it QLS-215 for hereditary angioedema.

- **Gene editing** – A study, published in ***Nature Communications***, found that TALEN is up to 5 times more efficient than CRISPR/Cas9, particularly for editing hard-to-edit genomic regions.

- **IONIS PHARMACEUTICALS** is collaborating with the University of California San Diego on an antisense approach to treating treatment-resistant multiple myeloma.

- **ITERUM THERAPEUTICS' sulopenem etzadroxil/probenecid (oral sulopenem)** – An NDA was accepted for review by the FDA to treat uncomplicated urinary tract infections (UTIs) in patients with a pathogen not susceptible to quinolone. The PDUFA date is July 25, 2021. An FDA advisory committee review is expected before the PDUFA date.

- **KOMODO HEALTH** is collaborating with **Blue Health Intelligence** to use its real-world patient data in its map of the U.S. healthcare system, so trial patients can be better tracked.

- **LILLY** licensed the exclusive rights to **Asahi Kasei Pharma's AK-1780**, an orally bioavailable P2X7 receptor antagonist for chronic pain.

- **MEDIGENE's MDG-1021** – Development was discontinued for this T cell receptor-modified (TCR-T) immunotherapy for relapsed/persistent hematologic cancers after a hematopoietic stem cell transplant.

- **MERCK MSD** is collaborating with **Artiva Biotherapeutics** to use Artiva's off-the-shelf CAR-NK cell manufacturing platform, starting with two undisclosed solid tumor targets.

- **MYOVANT SCIENCES and PFIZER's Orgovyx (relugolix)** – One-year data from the Phase III SPIRIT extension study of this oral gonadotropin-releasing hormone (GnRH) receptor antagonist, in women with endometriosis found clinically meaningful reductions in dysmenorrhea (menstrual pain) and in non-menstrual pelvic pain at Week 52, with minimal and stable bone mineral density loss.

- **NESTLÉ** is collaborating with **Senda Biosciences** on metabolics.

- **NEVAKAR's NVK-002 (atropine)** – The European rights to this eye drop for slowing the progression of myopia in children were licensed to **Laboratoires Théa**.

- **NOVARTIS' inclisiran** – The Institute for Clinical and Economic Review (ICER) said this siRNA for hypercholesterolemia needs to be priced between $3,600 and $6,000 a year to be cost-effective, but Novartis hasn't yet said how it will price the drug. ICER said the twice-yearly dosing is an advantage but compliance with that regimen is "an untested assumption."

- **PFIZER's Xeljanz (tofacitinib)**, a JAK inhibitor, missed the two co-primary endpoints in the FDA-mandated post-marketing ORAL Surveillance trial in rheumatoid arthritis, with both doses failing to show non-inferiority to TNF inhibitors in cardiovascular risk and in cancer risk with both doses tested. Translation: Xeljanz had *worse* safety.

- **PROTOLABS** bought **3D Hubs**, an online manufacturing platform.

- **REVANCE THERAPEUTICS' daxibotulinumtoxinA** – Data presented at the hybrid Maui Derm for Dermatologists 2021 meeting in Hawaii included an open-label Phase II trial which showed that different moderate-to-severe upper facial lines (glabellar, forehead, and lateral canthal lines) can be treated simultaneously; and a secondary analysis of the Phase III SAKURA trial showing a progressive effect of this toxin with a second and repeated treatments.

- **RHYTHM PHARMACEUTICALS' Imcivree (setmelanotide)** – Interim 3-month results of an ongoing Phase II basket trial in rare genetic forms of obesity (with variants in the MC4R pathway) showed subcutaneous administration of this MC4R agonist led to clinically meaningful weight loss, with 34.3% of patients achieving ≥5% weight loss. Responders also had a significant reduction in hunger vs. non-responders.

- **ROCHE's faricimab**, a bispecific (Ang2 + VEGF) antibody given Q8W, Q12W, or Q16W, met the primary endpoint in two identical Phase III trials – the 671-patient TENAYA and the 658-patient LUCERNE trials – in wet age-related macular degeneration (AMD), showing non-inferiority on visual acuity to Regeneron's Eylea (aflibercept) given Q8W.

- **SANOFI** – In a joint effort with Capgemini (a tech company), Generali France (an insurance company), and Orange (a telecom), Sanofi plans to work to use pooled digital resources to drive healthcare solutions in France.

- **VERTEX PHARMACEUTICALS' VX-880** – The FDA approved an investigational new drug (IND) application for this stem-cell-derived pancreatic islet cell therapy, clearing the way for a Phase I trial in Type 1 diabetes.

- **VIR BIOTECHNOLOGY's VIR-3434** – In top-line data from the first blinded cohort in an ongoing Phase I trial, 6 of 8 hepatitis B virus (HBV) patients who got this HBV-neutralizing antibody achieved a 1.3 $\log_{10}$ IU/mL reduction in HBV surface antigen (HBsAg) by Day 8.

Very early research news

- **Prostate cancer** – Researchers at the Asan Medical Center and the Biomaterials Research Center at the Korea Institute of Science and Technology have developed a smart biosensor that can detect prostate cancer with nearly 100% accuracy via urine.

NEWS IN BRIEF

ASTRAZENECA

- **Calquence (acalabrutinib)**, a BTK inhibitor, met the primary endpoint in the Phase III ELEVATE-RR trial, showing non-inferiority on progression-free survival (PFS) to Johnson & Johnson's Imbruvica (ibrutinib) in previously-treated, high-risk chronic lymphocytic leukemia (CLL). Calquence met a key safety secondary endpoint, with a significantly lower rate (that met superiority) of atrial fibrillation.

- Added the first target (so-far not identified) generated out of its artificial intelligence collaboration with **BenevolentAI**.

- Is collaborating with **Care Access Research** on Covid-19 antibody virtual trial work.

BEIGENE's tislelizumab

- This PD-1 inhibitor met the primary endpoint in the 512-patient Phase III RATIONALE-302 trial in advanced unresectable/metastatic esophageal squamous cell carcinoma, significantly improving overall survival vs. chemotherapy.

- The rights in North America, Europe, Japan, and Russia were sold to Novartis.

BIOGEN

- **and EISAI's aducanumab (BIIB-037).** The FDA extended the review of this antibody for treating Alzheimer's disease by three months after Biogen submitted new information requested by the FDA, considered a "major amendment." The new PDUFA date is June 7, 2021.

- **Tecfidera (dimethyl fumarate).** The 2.5-year results of the 22-patient Phase II FOCUS extension study, published in ***Frontiers in Neurology***, showed that long-term treatment with 240 mg BID orally is safe in pediatric patients with relapsing-remitting multiple sclerosis.

JOHNSON & JOHNSON

- **AURIS HEALTH's Monarch.** The results of the 55-patient BENEFIT trial, published in the journal ***CHEST***, showed that this robotic bronchoscopy system could localize and diagnose difficult-to-reach nodules at a higher rate than previously possible.

- **JANSSEN** is collaborating with **Verana Health** on research in ophthalmology and urology.

REGULATORY NEWS

Regulatory tidbits

- **FDA**
  - **Guidances.** The Center for Drug Evaluation and Research (CDER) issued a list of 42 new and 63 revised guidances that it plans to release in 2021. CDER also established four new categories of draft guidances: animal rule, biosimilars, compounding, and pharmacology/toxicology.
  - **Covid-19.** In updated guidance on trial exclusion criteria, the FDA said that Covid-19 treatments and vaccines that were granted emergency use authorization will not be considered investigational and thus patients on any of these drugs will not be excluded from participation in other trials.

- **Insulin** – President Biden signed an executive order that ***delayed*** until March 22, 2021, a final rule compelling community health centers receiving Section 330e grants who also participate in the 340B program, from providing insulin and injectable epinephrine at discounted prices to underprivileged patients. The delay was to give the new administration time to review the rule.

- **MERCK MSD's Propecia (finasteride)** – A judge granted ***Reuters*** request that Merck unseal documents from lawsuits over this baldness drug.

- **Opioids** – In the last days of the Trump Administration, the Department of Health and Human Services (HHS) announced plans to drop the X-waiver requirement for buprenorphine prescriptions, allowing physicians to more easily prescribe the drug for opioid use disorder (OUD). However, President Biden's HHS canceled that plan, saying HHS does not have the authority to waive the training requirements required before a physician can prescribe buprenorphine.

- **STIs** – In an analysis, published in the journal ***Sexually Transmitted Diseases***, the Centers for Disease Control and Prevention (CDC) estimated that in 2018, on any given day, 20% of Americans had a sexually transmitted infection (STI), with nearly 68 million STIs on any given day in 2018, 26 million newly acquired STIs (with nearly 50% of these in people age 15-24).

- **Telehealth** – South Dakota Gov. Kristi Noem is supporting legislation that would make two executive orders on telehealth permanent – one eliminating requirements for an in-person exam prior to telehealth use, another that would allow voice-only interactions, one allowing prescribing via telehealth, and a fourth recognizing out-of-state medical licenses under the Uniform Emergency Management Assistance Compact.

FDA approvals/clearances

- **ABBOTT's i-STAT Alinity TBI plasma assay** – The FDA gave the U.S. Army approval to use this traumatic brain injury test on the battlefield.

- **BOSTON SCIENTIFIC's Vercise Genus** – A fourth-generation version of this deep brain stimulation (DBS) system, was approved as an adjunctive therapy to reduce symptoms in moderate-to-advanced levodopa-responsive Parkinson's disease not adequately controlled with medication.

- **CHOICESPINE's Tiger Shark Cervical Spacer System** – An expanded line of spacer sizes was granted 510(k) clearance for use in spinal surgeries in patients with degenerative disc disease.

- **INSPIRED SPINE's Trident**, a sacroiliac joint-screw system for treating back pain, was granted 510(k) clearance.

- **LONGEVITI NEURO SOLUTIONS' Clearfit**, a cranial implant for use in postoperative ultrasound imaging, was granted 510(k) clearance.

- **MEDTRONIC's DiamondTemp Ablation (DTA)** system, a temperature-controlled open-irrigated radiofrequency (RF) ablation system, for treating recurrent, symptomatic paroxysmal atrial fibrillation (AF) patients who have been unresponsive to drug therapy, was cleared for use.

- **ORTHOSPIN's Generation 2 OrthoSpin system**, a robotic, digitally-enabled external fixation system for orthopedic treatments, was cleared for use.

- **SIEMENS HEALTHINEERS' Multix Impact C**, a ceiling-mounted digital radiography system, and **Multix Impact VA20**, a new version of the floor-mounted parent digital radiography system, were cleared for use.

- **THERANICA's Nerivio**, a remote electrical neuromodulation device, was granted expanded approval to include treatment of chronic and episodic migraines in pediatric patients age ≥12.

FDA recalls/warnings

- **The Body Building** received an untitled letter from the FDA's Center for Biologics Evaluation and Research (CBER) for marketing regenerative medicine (stem cell) products with unsubstantiated claims that they can treat a variety of conditions, including reversing the effects of autoimmune diseases.

- **EDGE PHARMA** received an untitled letter from CBER about its marketing of "patient-specific immunotherapy" vials without a license.

- **Hand sanitizers** – The FDA put ***all*** hand sanitizers from Mexico on import alert to help prevent import of products contaminated with methanol.

- **LONZA** got a Form 483 (with 4 observations) for its Texas plant. This is the plant that has caused the delay in approval of Bristol-Myers Squibb/Celgene/Juno Therapeutics' liso-cabtagene maraleucel (JCAR-017, liso-cel) for diffuse large B-cell lymphoma (DLBCL).

- **MEITHEAL PHARMACEUTICALS' cisatracurium besylate** – A single lot of this muscle-relaxer that is used in surgery was recalled due to some vials being incorrectly labeled as phenylephrine, an anti-hypertensive.

- **NOSTRUM LABORATORIES' metformin** – The recall due to NDMA contamination was expanded.

- **OLYMPUS' EndoTherapy** – The company voluntarily recalled ~26,000 of these disposable devices due to a packaging defect that could affect their sterility.

- **Professional Compounding Centers of America** got a warning letter for receiving and distributing adulterated and misbranded active pharmaceutical ingredients (APIs), including from at least one supplier on the import alert list.

European Regulatory News

- **AKTIIA**'s wearable, automated blood pressure-monitoring device was granted a CE Mark.
- **AMARIN PHARMACEUTICALS' Vazkepa (icosapent ethyl)** – The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended approval of this fish oil to reduce cardiovascular events in patients at high cardiovascular risk.
- **ARVELLE THERAPEUTICS' Ontozry (cenobamate)** – CHMP recommended approval to treat adult epilepsy not adequately controlled despite a history of treatment with ≥2 anti-epileptics.
- **ASTRAZENECA's AZD-1222**, a Covid-19 vaccine, was granted conditional marketing authorization by the European Commission.
- **INCYTE's Pemazyre (pemigatinib)** – CHMP recommended approval as a second-line treatment for advanced/metastatic cholangiocarcinoma with an FGFR2 fusion/rearrangement.
- **KARYOPHARM's Nexpovio (selinexor)** – CHMP recommended approval to treat relapsed/refractory multiple myeloma.
- **MABXIENCE RESEARCH's Alymsys (bevacizumab)** – a biosimilar of **Roche's Avastin** – CHMP recommended approval to treat carcinoma of the colon or rectum, breast cancer, NSCLC, renal cell cancer, epithelial ovarian, fallopian tube, primary peritoneal cancer, and carcinoma of the cervix.
- **MEDIBIO's MEBsleep**, artificial intelligence-based sleep-stage analysis software, was granted a CE Mark.
- **NOVARTIS' Kesimpta (ofatumumab)** – CHMP recommended approval to treat relapsing forms of multiple sclerosis.
- **NOVO NORDISK's Sogroya (somapacitan)** – CHMP recommended approval to treat growth hormone deficiency in adults.
- **PAION's Byfavo (remimazolam)** – CHMP recommended approval for use as a procedural sedative.
- **STADA ARZNEIMITTEL's Oyavas (bevacizumab)** – a biosimilar of **Roche's Avastin** – CHMP recommended approval to treat carcinoma of the colon or rectum, breast cancer, NSCLC, renal cell cancer, epithelial ovarian, fallopian tube, primary peritoneal cancer, and carcinoma of the cervix.
- **TEVA**
  - **BroPari Spiromax (salmeterol + fluticasone)** – CHMP recommended approval to treat asthma.
  - **Seffalair Spiromax (salmeterol + fluticasone)** – CHMP recommended approval to treat asthma.
- **ZIMMER BIOMET**'s Bactiguard-coated orthopedic trauma implants were granted a CE Mark.

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

- **BRISTOL-MYERS SQUIBB/CELGENE's Revlimid (lenalidomide)** – NICE reversed itself and now says Revlimid can be used as maintenance therapy for patients with newly-diagnosed multiple myeloma after a stem cell transplant.

Regulatory news from other countries

- ***Japan.*** **MALLINCKRODT's Cellex**, an extracorporeal photopheresis (ECP) system for treating steroid-resistant/intolerant chronic graft-versus-host disease (cGvHD) in adults, was approved by the Ministry of Health, Labour, and Welfare (MHLW).

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*
January 27	**Protalix BioTherapeutics and Chiesi's pegunigalsidase alfa** (PRX-102) for Fabry disease	PDUFA date **No decision announced yet**
January 28	**Amgen's Nplate** (romiplostim) – expanded approval to treat hematopoietic syndrome of acute radiation syndrome	PDUFA date **No decision announced yet**
Upcoming for 2021		
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	Research on barriers and solutions to **oral anti-cancer agent adherence**	FDA-ASCO virtual workshop
February 8	Review of **AstraZeneca's AZD-1222** Covid-19 vaccine	World Health Organization's Strategic Advisory Group of Experts on Immunization (SAGE) virtual meeting ***– tentative***
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 9-11	Development of **pediatric medical devices**	FDA, AdvaMed, the Critical Path Institute, and the American Academy of Pediatrics joint virtual public 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 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 **Extended by FDA to June 7**
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 tba	**Roche's Esbriet** (pirfenidone) – expanded approval to treat unclassifiable interstitial lung disease	PDUFA date
May 14	**Apellis Pharmaceuticals' pegcetacoplan** for treating PNH	PDUFA date
May 18	**Sanofi's avalglucosidase alfa** for Pompe disease	PDUFA date
May 20	**Bristol-Myers Squibb's Opdivo** (nivolumab) – expanded approval as adjuvant therapy for resected esophageal or gastroesophagel junction cancer	PDUFA date
May 21	**ADC Therapeutics' loncastuximab tesirine** for relapsed/refractory DLBCL	PDUFA date
May 25	**Bristol-Myers Squibb's Opdivo** (nivolumab) – expanded approval for use in combination with chemotherapy as a first-line treatment for gastric cancer	PDUFA date
May 30	**Kadmon's belumosudil** for chronic graft-versus-host disease after hematopoietic stem cell transplant	PDUFA date
June 7	**Biogen and Eisai's aducanumab** for Alzheimer's disease	PDUFA date **Extended 3 months by FDA from March 7**
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

2021 FDA Advisory Committees and Other Regulatory Dates of Interest – *continued* *RED are new since last week*		
Date	**Topic**	**Committee/Event**
July tba	**Bayer's finerenone** (BAY-94-8862) for Type 2 diabetes patients with CKD	PDUFA date
July 2	**Provention Bio's teplizumab** (PRV-031) for preventing/delaying clinical Type 1 diabetes	PDUFA date
July 18	**Merck MSD's V114**, a 15-valen pneumococcal conjugate vaccine	PDUFA date
July 20	**Albireo Pharma's odevixibat** (A-4250) to treat pruritus in patients with progressive familial intrahepatic cholestasis (PFIC)	PDUFA date
July 25	**Iterum Therapeutics' sulopenem etzadroxil/probenecid** for uncomplicated urinary tract infections	PDUFA date
October tba	**Pfizer and OPKO Health's somatrogon** for growth hormone deficiency	PDUFA date