NEW DRUG APPROVALS

Qtern for Type-2 Diabetes

The FDA has approved AstraZeneca's Qtern (dapagliflozin 10 mg [Farxiga] and saxagliptin 5 mg [Onglyza]) as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes who have inadequate control with dapagliflozin (10 mg) or who are already treated with dapagliflozin and saxagliptin.

Qtern combines two antihyperglycemic agents with complementary mechanisms of action in a once-daily tablet: dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, and saxagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor. SGLT2 inhibitors help patients achieve improved glycemic control by reducing the reabsorption of glucose from the blood and enabling its removal via the urine. DPP-4 inhibitors reduce blood glucose.

Source: AstraZeneca, February 28, 2017

Siliq for Psoriasis

Brodalumab injection (Siliq, Valeant Pharmaceuticals) has received FDA approval for the treatment of adults with moderate-to-severe plaque psoriasis. Brodalumab is intended for patients who are candidates for systemic therapy or phototherapy and have failed to respond or have stopped responding to other systemic therapies.

The efficacy and safety of brodalumab were established in three randomized, placebo-controlled trials involving 4,373 adults with moderate-to-severe plaque psoriasis who were candidates for systemic therapy or phototherapy. A greater number of patients treated with brodalumab had skin that was rated "clear" or "almost clear" compared with the placebo-treated patients.

Source: Valeant Pharmaceuticals, February 16, 2017

Emflaza for Duchenne Muscular Dystrophy

The FDA has approved deflazacort (Emflaza, Marathon Pharmaceuticals) tablets and oral suspension for the treatment of patients 5 years of age and older with Duchenne muscular dystrophy (DMD), a rare genetic disorder that causes progressive muscle deterioration and weakness. Deflazacort is a corticosteroid that works by reducing both inflammation and the activity of the immune system.

The efficacy of deflazacort was demonstrated in a study involving 196 boys 5–15 years of age at the beginning of the trial with a documented mutation of the dystrophin gene and the onset of weakness before age 5. At week 12, patients treated with deflazacort showed improvements in a clinical assessment of muscle strength across a number of muscles compared with patients receiving placebo. An overall stability in average muscle strength was maintained through the end of study at week 52 in the deflazacort-treated patients.

Source: Marathon Pharmaceuticals, February 9, 2017

Parsabiv for Hyperparathyroidism In Adults on Hemodialysis

Etelcalcetide (Parsabiv, Amgen) has secured FDA approval for the treatment of secondary hyperparathyroidism in adults with chronic kidney disease on hemodialysis. Etelcalcetide is the first therapy approved for this condition in 12 years. In addition, it is the only calcimimetic that can be administered intravenously by the dialysis team three times a week at the end of the hemodialysis session, according to Amgen.

Two 26-week, phase 3, randomized, double-blind trials showed that significantly more etelcalcetide-treated patients than placebo-treated patients achieved a reduction of greater than 30% from baseline in parathyroid hormone (PTH) during weeks 20–27: 77% versus 11%, respectively, in study 1, and 79% versus 11% in study 2. In addition, more patients in the etelcalcetide group than in the placebo group achieved PTH levels of 300 pg/mL or less: 52% versus 6%, respectively, in study 1, and 56% versus 5% in study 2.

Source: Amgen, February 8, 2017

Xermelo for Carcinoid Syndrome Diarrhea

The FDA has green-lighted telotristat ethyl (Xermelo, Lexicon Pharmaceuticals) as the first orally administered therapy for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analogue (SSA) therapy in adults inadequately controlled by SSA therapy alone. Carcinoid syndrome is a rare, debilitating condition that affects patients with metastatic neuroendocrine tumors (mNETs). Telotristat targets the overproduction of serotonin inside mNET cells. The treatment became available in select specialty pharmacies on March 6, 2017.

Source: Lexicon Pharmaceuticals, February 28, 2017

Generic Approvals and Launches

Desvenlafaxine ER Tablets

Teva Pharmaceutical Industries has announced the U.S. launch of desvenlafaxine extended-release (ER) 25-mg, 50-mg, and 100-mg tablets—the generic version of Pristiq (Pfizer)—for the treatment of patients with major depressive disorder (MDD). Desvenlafaxine is a serotonin and norepinephrine reuptake inhibitor. The efficacy of desvenlafaxine ER tablets was established in four short-term (eight-week) placebo-controlled studies and in two maintenance studies in adult outpatients with MDD.

Source: Teva Pharmaceutical, March 1, 2017

Testosterone Topical Solution

Perrigo Company has received final approval from the FDA for its abbreviated new drug application referencing Eli Lilly and Company's Axiron topical solution, 30 mg/1.5 mL (testosterone topical solution, 30 mg/1.5 mL). Axiron topical solution is indicated to treat men who have low or no testosterone due to certain medical conditions.

Source: Perrigo Company, March 1, 2017

Oxycodone/Acetaminophen Tablets

Lupin Ltd. has received final FDA approval for its oxycodone and acetaminophen tablets USP, 2.5 mg/325 mg, 5 mg/325 mg, 7.5 mg/325 mg, and 10 mg/325 mg. Lupin's product is the generic equivalent of Percocet tablets (Vintage Pharmaceuticals). The generic product is indicated for the relief of moderate to moderately severe pain.

Source: Lupin Ltd., February 28, 2017

Butalbital/Acetaminophen Tablets

Butalbital/acetaminophen tablets 50 mg/300 mg, indicated for the treatment of tension headache (migraine), have been launched in the United States. Mayne Pharma will distribute the drug on behalf of its partner, Mikart, Inc.

Source: Mayne Pharma, February 16, 2017

NEW INDICATIONS

Revlimid for Post-HSCT Maintenance in Myeloma

The FDA has expanded the existing indications for lenalidomide (Revlimid, Celgene Corporation), a thalidomide analogue, to include use in patients with multiple myeloma as maintenance therapy after autologous hematopoietic stem cell transplant (auto-HSCT). The expanded indication makes lenalidomide the only treatment to receive FDA approval for maintenance use following auto-HSCT.

Lenalidomide in combination with dexamethasone was approved in June 2006 for patients with multiple myeloma who have received at least one prior therapy. It is also indicated for patients with transfusion-dependent anemia due to low- or intermediate-1–risk myelodysplastic syndromes associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities, and for patients with mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

Source: Celgene, February 22, 2017

Spiriva Respimat for Asthma

The FDA has approved Spiriva Respimat (tiotropium bromide, Boehringer Ingelheim), a steroid-free inhalation spray, for the long-term, once-daily maintenance treatment of asthma in patients 6 years of age and older. The product was originally approved in September 2015 for the long-term, once-daily maintenance treatment of asthma in patients 12 years of age and older.

The new approval was based on efficacy and safety data from the phase 2 and phase 3 UniTinA-asthma clinical development program, which included more than 6,000 patients worldwide, among them 804 children (6–11 years of age).

Source: Boehringer Ingelheim, February 16, 2017

Opdivo for Bladder Cancer

Nivolumab (Opdivo, Bristol-Myers Squibb) intravenous injection has been approved by the FDA for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or after platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. It is the eighth indication for the programmed death receptor-1–blocking antibody.

Source: Bristol-Myers Squibb, February 2, 2017

NEW FORMULATION

Gammaplex 10% for Immunodeficiency

Gammaplex 10% (immune globulin intravenous [human], 10% liquid, Bio Products Laboratory) has received FDA approval for the treatment of adults with primary immunodeficiency or chronic immune thrombocytopenic purpura. Gammaplex 10% is made with the same process as Bio Products' previously approved intravenous immunoglobulin treatment Gammaplex 5% (immune globulin intravenous [human], 5% liquid). Gammaplex 10% is more concentrated than Gammaplex 5%, with an immunoglobulin G concentration of 100 g/L, and is stabilized with glycine.

Source: Bio Products Laboratory, February 8, 2017

FDA REVIEW ACTIVITIES

Priority Review Designations

Avelumab for Urothelial Carcinoma

The FDA has accepted for priority review a biologics license application for avelumab (Merck/Pfizer) as a potential treatment for patients with locally advanced or metastatic urothelial carcinoma with disease progression during or after platinum-based therapy. The agency has set an action date of August 27, 2017.

Avelumab is a fully human antibody specific for programmed death ligand-1 (PD-L1). By inhibiting PD-L1 interactions, avelumab is believed to enable the activation of T cells and the adaptive immune system. By retaining a native Fc-region, avelumab is thought to potentially engage the innate immune system and induce antibody-dependent cell-mediated cytotoxicity.

Source: Merck, February 28, 2017

Zykadia for Lung Cancer

A supplemental new drug application for ceritinib (Zykadia, Novartis) has been accepted by the FDA. The agency has granted priority review for the expanded use of the drug as a first-line treatment for patients with metastatic non–small-cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive, as detected by an FDA-approved test. The FDA also granted breakthrough therapy status to ceritinib for the first-line treatment of patients with ALK-positive metastatic NSCLC with metastases to the brain.

Ceritinib is an oral, selective inhibitor of *ALK*, a gene that can fuse with other genes to form an abnormal "fusion protein" that promotes the development and growth of certain tumors, including NSCLC. Ceritinib is currently approved in more than 64 countries worldwide.

Source: Novartis, February 23, 2017

Inotuzumab Ozogamicin for ALL

A biologics license application for inotuzumab ozogamicin (Pfizer) has been accepted for filing and granted a priority review by the FDA. The compound is being evaluated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The goal date for an approval decision is in August.

Inotuzumab ozogamicin is an investigational antibody–drug conjugate consisting of a monoclonal antibody targeting CD22, a cell-surface antigen expressed on approximately 90% of B-cell malignancies, linked to a cytotoxic agent. When inotuzumab ozogamicin binds to the CD22 antigen on B cells, it is internalized into the cell, where the cytotoxic agent calicheamicin is released to destroy the cell.

Source: Pfizer, February 21, 2017

Glecaprevir/Pibrentasvir for Hepatitis C

The FDA has granted priority review of a new drug application (NDA) for the investigational, pan-genotypic regimen of glecaprevir/pibrentasvir (AbbVie) for the treatment of patients with all major genotypes (GT1–6) of chronic hepatitis C virus. The NDA was supported by data from eight registrational studies, which evaluated more than 2,300 patients in 27 countries. The fixed-dose combination of glecaprevir (100 mg), an NS3/4A protease inhibitor, and pibrentasvir (40 mg), an NS5A inhibitor, is dosed once-daily as three oral tablets (i.e., 300 mg/120 mg).

Source: AbbVie, February 2, 2017

Breakthrough Therapy Status

Toca 511/Toca FC for Glioma

The FDA has granted breakthrough therapy status to Toca 511/Toca FC (Tocagen, Inc.) for the treatment of patients with recurrent high-grade glioma. The product—a combination of an investigational biologic (Toca 511) and an investigational small molecule (Toca FC)—is being evaluated in an international, randomized, phase 2/3 clinical trial, which was designed to serve as a potential registrational study. The trial involves patients with first or second recurrence of glioblastoma or anaplastic astrocytoma who are undergoing resection. Enrollment in the phase 2 portion of the study has been completed, and top-line results are expected in the first half of 2018.

Source: Tocagen, February 23, 2017

Fast-Track Designations

ImmunoPulse IL-12 for Melanoma

OncoSec Medical, Inc., has received a fast-track designation from the FDA for its ImmunoPulse IL-12 (intratumoral IL-12 plus electroporation), a potentially first-in-class, intratumoral anticancer gene therapy that expresses interleukin-12 (IL-12) for the treatment of metastatic melanoma after progression during treatment with pembrolizumab or nivolumab.

The Anti–PD-1 IL-12 Stage III/IV Combination Electroporation Study (PISCES) will be a phase 2b, open-label, single-arm trial of ImmunoPulse IL-12 in combination with an intravenous anti–programmed death-1 (PD-1) antibody in patients with a histological diagnosis of melanoma with progressive, locally advanced, or metastatic disease (defined as stage III or stage IV). Eligible patients will be those with stage III/IV metastatic melanoma who are progressing or have progressed on or within 24 weeks of receiving approved anti–PD-1 antibodies during either pembrolizumab or nivolumab treatment (either as monotherapy or in combination with another approved checkpoint inhibitor). The trial's primary endpoint will be the overall response rate at 24 weeks.

Source: OncoSec Medical, February 27, 2017

Generx for Coronary Heart Disease

The FDA has granted fast-track status to a phase 3 clinical study of Generx (Ad5FGF-4, Angionetics, Inc.) cardiovascular angiogenic gene therapy as a one-time treatment for improving exercise tolerance in patients with angina that is refractory to standard medical therapy and is not amenable to conventional revascularization procedures (i.e., coronary artery bypass surgery and percutaneous coronary intervention). Generx is biologically engineered using an adenovirus serotype 5 vector.

Source: Angionetics, February 7, 2017

Orphan Drug Designation

EDV Nanocells for Glioblastoma Multiforme

The FDA has granted orphan drug status to bacteria-derived, epidermal growth factor receptor-targeted, doxorubicin-loaded EDV nanocells (EnGeneIC Ltd.)

for the treatment of patients with glioblastoma multiforme. EDV nanocells have been designed to target and kill tumor cells with minimal toxicity while stimulating the immune system's natural antitumor response. Intravenously injected EDV nanocells exit the leaky vascular system that is found only within tumors and attach to cancer cells via a targeted bispecific antibody. Once attached, the nanocell is able to enter the tumor cell and deliver a drug, short-interfering RNA, or microRNA payload at high concentrations, intracellularly.

Source: EnGeneIC, March 2, 2017

Complete Response Letter

Naloxone Nasal Spray For Opioid Overdose

The FDA has issued a complete response letter (CRL) regarding the new drug application (NDA) for naloxone hydrochloride 2.0 mg/0.5 mL nasal spray. Amphastar Pharmaceuticals is seeking approval of the product for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. The CRL identified several issues, including a human-factors study and a device evaluation, that need to be addressed before the NDA can be approved.

Naloxone hydrochloride, the N-allyl derivative of oxymorphone, is the standard of care for opioid overdose. It was first approved in 1971 to reverse opioid intoxication or overdose.

Source: Amphastar Pharmaceuticals, February 21, 2017

New or Revised Drug Applications

Sublingual Dsuvia for Acute Pain

The FDA has accepted a new drug application (NDA) for Dsuvia (sufentanil sublingual tablets, 30 mcg, AcelRx Pharmaceuticals) for the treatment of patients with moderate-to-severe acute pain in a medically supervised setting. The agency has set an action date of October 12, 2017.

Dsuvia is delivered sublingually by a health care professional using a disposable, prefilled, single-dose applicator.

Source: AcelRx Pharmaceuticals, February 27, 2017

Latanoprostene Bunod for Glaucoma

Bausch + Lomb (a subsidiary of Valeant Pharmaceuticals International) and Nicox S.A. have resubmitted a new drug application to the FDA seeking approval of latanoprostene bunod ophthalmic solution, 0.024%. Latanoprostene bunod is an intraocular pressure (IOP)–lowering single-agent eye drop dosed once daily for patients with open-angle glaucoma or ocular hypertension. Latanoprostene bunod is believed to lower IOP by increasing the outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes.

Source: Valeant Pharmaceuticals, February 27, 2017

Lotus Valve Heart Device

Boston Scientific has delayed the submission of its FDA marketing application for the Lotus Valve heart device to the fourth quarter of 2017, and said it expects to launch the product in the U.S. in mid 2018. The company had previously expected to submit the application in May 2017 and obtain the FDA's approval by the end of the year.

The action came after the company was obliged in February to withdraw the devices in Europe and elsewhere, citing reports of problems with the locking mechanism. The company had suspended implants of its next-generation Lotus Edge device in Europe in October 2016 over similar concerns, but said in January that it had found a fix for the problem.

Source: Reuters, February 23, 2017

Dextenza for Postsurgical Ocular Pain

A new drug application resubmission for Dextenza (dexamethasone insert, 0.4 mg, Ocular Therapeutix, Inc.) for the treatment of patients with ocular pain after ophthalmic surgery has been accepted for review by the FDA. Dextenza is a product candidate administered by a physician as a bioresorbable intracanalicular insert and is designed for drug release to the ocular surface for up to 30 days. The FDA has given the resubmission a target action date of July 19, 2017.

Source: Ocular Therapeutix, February 22, 2017

Biosimilar Pegfilgrastim

The FDA has accepted a biologics license application for MYL-1401H (Mylan/Biocon Ltd.), a proposed biosimilar to Neulasta (pegfilgrastim, Amgen). The proposed biosimilar is used to reduce the duration of neutropenia and the incidence of fever associated with neutropenia in adults treated with chemotherapy in certain types of cancer. The FDA goal date set under the Biosimilar User Fee Act is October 9, 2017.

Source: Mylan, February 16, 2017

Blincyto for ALL

Amgen has submitted a supplemental biologics license application (sBLA) to the FDA for blinatumomab (Blincyto) to include overall survival data from the phase 3 TOWER study, which support the conversion of blinatumomab accelerated approval to full approval. The sBLA also includes new data supporting the treatment of patients with Philadelphia chromosome-positive relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The application aims to broaden the indication for treatment with blinatumomab to patients with relapsed or refractory B-cell precursor ALL.

Source: Amgen, February 14, 2017

Zilretta for Osteoarthritic Knee Pain

The FDA has accepted a new drug application for Zilretta (Flexion Therapeutics), which is being evaluated as a potential intra-articular, extended-release treatment for the pain of osteoarthritis of the knee. The agency has established an action date of October 6, 2017. Zilretta employs a proprietary microsphere technology that combines a short-acting corticosteroid with a poly(lactic-co-glycolic acid) matrix.

Source: Flexion Therapeutics, February 7, 2017

Label Updates

Trulicity for Diabetes

The FDA has updated the label for once-weekly dulaglutide (Trulicity, Eli Lilly), an injectable glucagon-like peptide-1 (GLP-1) receptor agonist, to include use in combination with basal insulin in adults with type-2 diabetes. Dulaglutide is available in a prefilled pen in 0.75-mg and 1.5-mg doses.

The label update was based on an FDA review of results from the AWARD-9 trial, a phase 3b, randomized, double-blind, placebo-controlled, 28-week study that evaluated the efficacy and safety of once-weekly dulaglutide 1.5 mg as an add-on to titrated insulin glargine, with or without metformin, compared with placebo as an add-on to titrated insulin glargine, with or without metformin. In the study, dulaglutide 1.5 mg significantly reduced hemoglobin A1c as an add-on to insulin glargine after 28 weeks compared with placebo plus insulin glargine (1.4% versus 0.7%, respectively).

Source: Eli Lilly, February 8, 2017

Gel-One for Osteoarthritic Knee Pain

The FDA has approved an expanded 26-week efficacy claim for the single-injection viscosupplement Gel-One (cross-linked hyaluronate, Zimmer Biomet Holdings) for the treatment of patients with knee pain associated with osteoarthritis (OA). The product may be administered in the physician's office and is indicated for the treatment of knee pain in OA patients who have failed to respond adequately to nonpharmacological therapy, to nonsteroidal anti-inflammatory drugs, or to simple analgesics, such as acetaminophen. Gel-One is the first low-volume viscosupplement available in a single-injection formulation for the treatment of knee OA, according to the manufacturer.

Source: Zimmer Biomet Holdings, February 1, 2017

DRUG SAFETY ISSUES

MedWatch Alerts

The FDA has issued MedWatch Safety Alerts regarding the following products and devices:

- *Alaris Syringe Pump (CareFusion):* Faulty Air-In-Line sensor, which may generate a false alarm and cause the syringe pump to stop supplying the infusion to the patient. The interruption of infusion could lead to serious adverse health consequences or death. Posted February 9, 2017.
- *Chlorhexidine Gluconate:* Rare but serious reactions can occur within minutes of exposure and may include wheezing or difficulty breathing; swelling of the face; hives that can quickly progress to more serious symptoms; severe rash; or shock, a life-threatening condition. Posted February 2, 2017.
- *Halo One Thin-Walled Guiding Sheath (Bard Peripheral Vascular, Inc.):* The affected product may cause serious adverse health consequences, such as internal tears and perforation to arteries or veins, excessive bleeding, and death. Posted January 30, 2017.
- *ED-3490TK Duodenoscope (Pentax):* Updated recommendations to help prevent the spread of infection associated with the use of these devices. Posted January 17, 2017.

CLINICAL TRIAL NEWS

Ataluren for Cystic Fibrosis

PTC Therapeutics has announced that the ataluren confirmatory trial in patients with nonsense-mutation cystic fibrosis (CF) did not achieve its primary or secondary endpoints. The company has discontinued the clinical development of ataluren in patients with CF; has closed ongoing extension studies; and has withdrawn its application for marketing authorization in CF in Europe. Ataluren is a protein-restoration therapy designed to enable the formation of a functioning protein in patients with genetic disorders caused by a nonsense mutation.

Source: PTC Therapeutics, March 2, 2017

Drug Cocktail for Early Breast Cancer

Positive results have been reported from the phase 3 study of adjuvant treatment with the combination of pertuzumab (Perjeta), trastuzumab (Herceptin), and chemotherapy in patients with human epidermal growth factor receptor 2–positive early breast cancer. The combination regimen achieved a statistically significant reduction in the risk of recurrence of invasive disease or death compared with trastuzumab and chemotherapy alone.

Pertuzumab and trastuzumab are marketed in the United States by Genentech, a member of the Roche group. The combination of pertuzumab, trastuzumab, and chemotherapy is currently available under the FDA's accelerated approval program.

Source: Roche, March 2, 2017

Blincyto for ALL

Positive results have been reported from the phase 3 TOWER study evaluating the efficacy of blinatumomab (Blincyto, Amgen) compared with that of standard-of-care (SoC) chemotherapy in high-risk adults with Philadelphia chromosome-negative, relapsed, or refractory B-cell precursor acute lymphoblastic leukemia (ALL)—one of the most aggressive B-cell malignancies. Results from the analysis showed that median overall survival was 7.7 months for blinatumomab compared with 4.0 months for SoC (hazard ratio for death, 0.71; $P = 0.012$). The TOWER trial is the confirmatory study for the phase 2 trial that supported the FDA's accelerated approval designation for blinatumomab in 2014.

Blinatumomab is a bispecific CD19-directed CD3 T-cell engager (BiTE) antibody construct. BiTE antibody constructs are currently being investigated for their potential to treat a variety of cancers.

Source: Amgen, March 1, 2017

AC-1204 for Alzheimer's Disease

Accera, Inc., has announced that patients with mild-to-moderate Alzheimer's disease treated with the company's small-molecule compound AC-1204 did not demonstrate a statistically significant difference at 26 weeks compared with patients given placebo, as measured by the Alzheimer's Disease Assessment Scale–Cognitive Subscale test. The formulation of AC-1204 was changed between phase 2 and phase 3 studies, and this change had the unintended consequence of lowering drug levels in patients, according to a company spokesperson. Accera intends to present an analysis of the new study at the Alzheimer's Association International Conference in London in July 2017.

Source: Accera, February 28, 2017

Letermovir for CMV Infection in Bone Marrow Transplant Recipients

Positive results have been reported from a pivotal phase 3 study of letermovir (Merck), an investigational antiviral medication for the prevention of clinically significant cytomegalovirus (CMV) infection in adult CMV-seropositive recipients of an allogeneic hematopoietic stem cell transplant (HSCT). The study met its primary efficacy endpoint, demonstrating that significantly fewer patients with undetectable CMV DNA at the start of treatment developed clinically significant CMV infection through week 24 post-HSCT. Letermovir prophylaxis was also associated with lower all-cause mortality through week 24 post-HSCT. Based on these results, Merck plans to submit a new drug application to the FDA in 2017.

Source: Merck, February 27, 2017

V212 Vaccine for Herpes Zoster

Merck has announced the first phase 3 study results for V212, the company's investigational inactivated varicella zoster virus (VZV) vaccine for the prevention of herpes zoster, also known as shingles, in immunocompromised patients. The double-blind, randomized, placebo-controlled trial evaluated the safety, tolerability, efficacy, and immunogenicity of inactivated VZV in recipients of autologous hematopoietic stem cell transplants (auto-HSCTs). V212 met the study's primary endpoint, reducing the incidence of confirmed herpes zoster cases by an estimated 64% in recipients of auto-HSCT.

Source: Merck, February 27, 2017

LJPC-501 for Hypotension

Positive results have been reported from a phase 3 trial of LJPC-501 (La Jolla Pharmaceutical Company) in patients with catecholamine-resistant hypotension (CRH). LJPC-501 is a proprietary formulation of synthetic human angiotensin II. Endogenous angiotensin II, the major bioactive component of the renin–angiotensin system, is one of the body's central regulators of blood pressure.

The ATHOS-3 trial was a randomized, double-blind, placebo-controlled study of LJPC-501 in 321 patients with CRH in nine countries. The primary efficacy endpoint was the percentage of patients with mean arterial pressure (MAP) of 75 mm Hg or greater or a 10-mm Hg increase from baseline MAP three hours after the initiation of study treatment without an increase in standard-of-care vasopressors.

The primary efficacy result was statistically significant: 70% of 163 patients treated with LJPC-501 showed a blood pressure response compared with 23% of 158 placebo-treated patients ($P < 0.00001$).

Source: La Jolla Pharmaceutical Company, February 27, 2017

Fusidic Acid for Skin Infections

Positive results have been reported from a phase 3 study of oral fusidic acid (Cempra, Inc.) in 716 patients with acute bacterial skin and skin-structure infections. Fusidic acid achieved the trial's primary endpoint, demonstrating noninferiority compared with oral linezolid for early clinical response (ECR). In the study, 87.2% of patients receiving fusidic acid demonstrated ECR compared with 86.6% of patients receiving linezolid. Fusidic acid is orally active against gram-positive bacteria, including *Staphylococcus aureus* strains.

Source: Cempra, February 24, 2017

Pradaxa Versus Warfarin In Real-World Study

Results from a real-world analysis have shown that dabigatran etexilate mesylate (Pradaxa, Boehringer Ingelheim) was associated with improved safety and efficacy outcomes compared with war-

farin in patients with nonvalvular atrial fibrillation (NVAF). The study analyzed 7,245 dabigatran-treated patients and 14,490 warfarin-treated patients with NVAF with no exposure to oral anticoagulants.

Compared with warfarin, dabigatran was associated with a 26% reduced risk of stroke (hazard ratio [HR], 0.74) and a 20% reduced risk of major bleeding (HR, 0.80). Dabigatran was also associated with a reduced risk of serious secondary outcomes, including a 68% reduced risk of hemorrhagic stroke (HR, 0.32), an 18% reduced risk of major extracranial bleeding (HR, 0.82), a 48% reduced risk of venous thromboembolism (HR, 0.52), and a 27% reduced risk of death (HR, 0.73).

Source: Boehringer Ingelheim, February 24, 2017

Emicizumab for Hemophilia

In a letter to the European Haemophilia Consortium, Roche has confirmed that one patient died in a phase 3 study of the bispecific antibody emicizumab. The death was considered to be unrelated to emicizumab, but, with the event following similar serious adverse events (SAEs) with other agents, it has added to questions about the safety of the experimental treatment.

Roche stated that it had received two reports of SAEs in a patient who was enrolled in the company's HAVEN 1 trial. The patient experienced a serious rectal hemorrhage (the first reported SAE) and received bypassing agents, after which the patient developed signs of thrombotic microangiopathy (TMA) (the second SAE). Treatment of the hemorrhage was complicated because the patient declined blood transfusions. The patient subsequently died.

The clinical and laboratory characteristics of this case of TMA were consistent with those observed in two previously reported cases involving Novo Nordisk's NovoSeven (coagulation factor VIIa [recombinant]) and Shire's Feiba (anti-inhibitor coagulant complex).

Sources: European Haemophilia Consortium, February 21, 2017; and *FierceBiotech,* February 24, 2017

Rocapuldencel-T For Kidney Cancer

An independent data-monitoring committee for the pivotal phase 3 ADAPT trial of rocapuldencel-T (Argos Therapeutics) in combination with sunitinib/standard-of-care for the treatment of patients with metastatic renal cell carcinoma has recommended that the trial be discontinued for futility, based on its planned interim data analysis. The committee concluded that the study was unlikely to demonstrate a statistically significant improvement in overall survival in the combination-treatment arm, the study's primary endpoint. The study was initiated in January 2013 and completed enrollment in July 2015.

Rocapuldencel-T is an individualized immunotherapy that is designed to capture mutated and variant antigens that are specific to each patient's tumor and induce an immune response targeting that patient's tumor antigens.

Source: Argos Therapeutics, February 22, 2017

Olinvo for Postsurgical Pain

Mixed results have been reported from two pivotal phase 3 studies of the opioid painkiller oliceridine (Olinvo, Trevena, Inc.) in patients with moderate-to-severe acute pain after bunionectomy or abdominoplasty. In both studies, all dose regimens achieved their primary endpoint of statistically greater analgesic efficacy compared with placebo, as measured by the responder rate. However, only two of the three doses were found to be as effective as morphine. Moreover, while oliceridine induced lower rates of nausea and vomiting and lower rates of depressed breathing, only one dose achieved a statistically significant effect.

Source: Trevena, February 21, 2017

Tivantinib for Liver Cancer

The phase 3 METIV-HCC trial of tivantinib (ArQule, Inc./Daiichi Sankyo) in patients with hepatocellular carcinoma (HCC) did not meet its primary endpoint of improving overall survival. Tivantinib is an oral selective inhibitor of the c-MET receptor tyrosine kinase for second-line treatment of patients with MET-overexpressing hepatocellular carcinoma.

The METIV-HCC trial was a biomarker-selected, double-blind, placebo-controlled, randomized study evaluating tivantinib versus best supportive care in patients with MET-overexpressing, inoperable HCC intolerant to or previously treated with systemic therapy. A total of 340 patients with MET-overexpressing HCC were randomly assigned to the intent-to-treat population for the efficacy analysis.

Source: ArQule, February 17, 2017

Stelara for Crohn's Disease

Two-year data have been reported from the ongoing IM-UNITI long-term extension (LTE) study evaluating the efficacy and safety of subcutaneous ustekinumab (Stelara, Janssen Biotech) in adults with moderately to severely active Crohn's disease (CD). The data showed that treatment with ustekinumab maintained clinical response and remission for up to two years, with no new safety signals observed.

Among 397 randomized patients who entered the LTE period and continued to receive ustekinumab through week 96, 79% (61 of 77) receiving ustekinumab every 12 weeks and 87% (61 of 70) receiving ustekinumab every eight weeks were in remission, whereas 91% (70 of 77) and 94% (66 of 70) of patients showed a clinical response at week 92, respectively.

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Among all ustekinumab-treated patients who continued to receive ustekinumab through week 96, remission and response rates at week 92 were 71% (365 of 516) and 85% (437 of 516), respectively.

Source: Janssen, February 17, 2017

Baricitinib for RA

Additional results have been reported from a pivotal phase 3 study of baricitinib (Eli Lilly/Incyte Corp.) in the treatment of patients with moderate-to-severe rheumatoid arthritis (RA). Supplementary data from the RA-BEAM trial showed that, starting as early as week 8 and sustained through week 52, a greater proportion of patients treated with baricitinib achieved American College of Rheumatology (ACR) 50 and ACR70 responses—composite scores that represent at least 50% and 70% improvement, respectively, in multiple components of RA disease activity—compared with adalimumab (Humira, AbbVie). These improvements were statistically significant compared with adalimumab at weeks 12, 20, 28, 32, and 40.

Source: Eli Lilly, February 15, 2017

Tenapanor for Hyperphosphatemia

A phase 3 study evaluating the efficacy and safety of tenapanor (Ardelyx, Inc.) as a treatment for hyperphosphatemia in patients with end-stage renal disease who are on dialysis has met its primary endpoint.

The study demonstrated a statistically significant difference in serum phosphorus levels from the end of the eight-week treatment period to the end of the four-week randomized withdrawal period between the tenapanor-treated group and the placebo-treated group in 80 responder patients (mean, –1.01 mg/dL) and met its primary endpoint (least squares mean, –0.82 mg/dL; $P = 0.01$).

In hyperphosphatemia, tenapanor blocks the NHE3 sodium transporter in the gastrointestinal (GI) tract, reducing the absorption of dietary sodium and resulting in increased protons within the cells. This increase in protons causes a reduction in phosphate uptake by tightening junctions or pores that regulate phosphate absorption in the GI tract.

Source: Ardelyx, February 15, 2017

Genvoya for HIV-1 Infection

Positive 144-week data have been reported from two phase 3 studies of Genvoya (elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir alafenamide 10 mg, Gilead Sciences) for the treatment of human immunodeficiency virus-1 (HIV-1) infection in treatment-naïve adults. Through week 144, Genvoya demonstrated significantly higher rates of virological suppression compared with Stribild (elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg, Gilead), based on the percentage of patients with HIV-1 RNA levels of less than 50 copies/mL.

Genvoya is indicated for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (i.e., HIV-1 RNA levels of less than 50 copies/mL) on a stable antiretroviral regimen for at least six months, with no history of treatment failure and no known resistance to the components of Genvoya.

Source: Gilead Sciences, February 14, 2017

Dolutegravir/Rilpivirine For HIV Infection

Positive results have been reported from two phase 3 studies evaluating the safety and efficacy of switching virologically suppressed patients from a three- or four-drug antiretroviral regimen to the two-drug regimen of dolutegravir (ViiV Healthcare) and rilpivirine (Janssen). If approved, this treatment could be the first two-drug regimen for human immunodeficiency virus (HIV) infection and could offer patients infected with HIV who are virally suppressed the option of switching to a regimen that does not include a nucleotide reverse transcriptase inhibitor.

The dolutegravir/rilpivirine regimen achieved noninferior viral suppression (HIV-1 RNA less than 50 copies/mL) at 48 weeks compared with a three- or four-drug regimen in both pooled and individual analyses of the SWORD 1 and SWORD 2 studies (current antiretroviral therapy, 95% [485 of 511] versus dolutegravir/rilpivirine, 95% [486 of 513]; adjusted difference, –0.2% pooled analysis).

Source: Janssen Sciences Ireland, February 13, 2017

M207 Migraine Patch

M207 (Zosano Pharma) has achieved the coprimary endpoints of freedom from migraine pain and freedom from the most bothersome symptom of migraine at two hours in a pivotal phase 3 trial. M207 is a proprietary zolmitriptan-coated microneedle patch that delivers subcutaneous zolmitriptan during a migraine attack. Key findings included:

- 42% of treated patients experienced freedom from pain at two hours compared with 14% of the placebo group ($P < 0.0001$).
- 68% of treated patients experienced freedom from the most bothersome symptom of migraine at two hours compared with 43% of the placebo group ($P < 0.0009$).
- 27% of treated patients experienced freedom from pain at one hour compared with 10% of the placebo group ($P < 0.0084$).

Source: Zosano Pharma, February 13, 2017

Baremsis for PONV

Positive results have been announced from the fourth and final pivotal study of amisulpride injection (Baremsis, Acacia Pharma Group) for the rescue treatment of patients who develop postoperative nausea and vomiting (PONV) despite having received prior antiemetic prophylaxis. The phase 3, double-blind study compared two doses of amisulpride, a dopamine D_2/D_3 antagonist antiemetic, with placebo in 705 patients who experienced PONV. The optimal dose of amisulpride significantly improved the complete response rate compared with placebo ($P = 0.003$). A new drug application is expected in the first half of 2017.

Source: Acacia Pharma Group, February 13, 2017

Tecarfarin Oral Anticoagulant

The FDA is requiring Armetheon, Inc., to conduct a 1,000-patient pivotal trial for its drug candidate tecarfarin before the company can file a new drug application, which is projected to occur in 2019. Tecarfarin is being developed as a potential oral anticoagulant therapy for patients who require anticoagulation with a vitamin K antagonist, such as warfarin. This includes patients with prosthetic heart valves, repeat deep vein thrombosis, or chronic kidney disease. The new study will enroll patients with all indications for anticoagulation in order to support a broad label if the product is approved.

Source: Armetheon, February 9, 2017

Piclidenoson for RA

Can-Fite BioPharma has begun enrollment into a global phase 3 trial of piclidenoson as a first-line treatment, replacing methotrexate (MTX), in patients with rheumatoid arthritis (RA). The study is designed to enroll approximately 500 patients in Europe, Canada, and Israel. The primary endpoint of the 24-week, randomized, double-blind, active- and placebo-controlled trial is low disease activity after 12 weeks in RA patients treated with piclidenoson compared with those treated with MTX. Piclidenoson (1 mg or 2 mg) or placebo will be administered twice daily, and MTX or placebo will be administered once weekly. Piclidenoson is a first-in-class A3 adenosine receptor agonist small-molecule, orally bioavailable drug.

Source: Can-Fite BioPharma, February 8, 2017

Relugolix for Prostate Cancer

Myovant Sciences has initiated a phase 3 clinical trial to evaluate the safety and efficacy of relugolix in men with advanced prostate cancer. Relugolix is an oral, once-daily, small-molecule, gonadotropin-releasing hormone receptor antagonist that lowers testosterone by inhibiting the release of luteinizing hormone and follicle-stimulating hormone by the pituitary.

Approximately 1,125 patients will be enrolled in North and South America, Europe, and the Asia-Pacific region. The patients will be randomly assigned to receive oral relugolix (120 mg once daily) or a three-month depot injection of leuprolide acetate. The primary efficacy outcome will be the ability of relugolix to achieve and maintain serum testosterone suppression to castrate levels (less than or equal to 50 ng/dL [1.7 nmol/L]) for 48 weeks in patients with androgen-sensitive advanced prostate cancer.

Source: Myovant Sciences, March 1, 2017

RGN-137 for Epidermolysis Bullosa

GtreeBNT Co., Ltd., has received a positive response from the FDA regarding its phase 3 clinical trial design for RGN-137 in patients with epidermolysis bullosa (EB). RGN-137 is a dermal wound-healing gel that incorporates thymosin beta 4 as the active pharmaceutical ingredient. GtreeBNT is planning to initiate the phase 3 trial in the U.S. during the third quarter of 2017.

According to GtreeBNT, RGN-137 has the potential to reduce pain in patients with EB by accelerating wound healing, reducing inflammation, and upregulating the production of laminin-5, a protein that affects tissue integrity throughout the body. This protein is defective in patients with EB. RGN-137 has also been shown to reduce scarring in animals—another problem affecting EB patients.

GtreeBNT is developing RGN-137 in the U.S. under license from RegeneRx Biopharmaceuticals.

Source: RegeneRx Biopharmaceuticals, February 28, 2017

Larotrectinib for Solid Tumors

Loxo Oncology, Inc., has completed clinical trial enrollment for the new drug application (NDA) primary efficacy analysis of larotrectinib. The company expects to report top-line data for the NDA data set in the second half of 2017 and expects to submit an NDA in late 2017 or early 2018.

Larotrectinib is an oral investigational drug in clinical development for the treatment of patients with cancers that harbor abnormalities involving the tropomyosin receptor kinases (TRKs). Research suggests that *NTRK* genes, which encode for TRKs, can become abnormally fused to other genes, resulting in growth signals that can lead to cancer in many sites of the body.

Source: Loxo Oncology, February 21, 2017

GS010 for Optic Neuropathy

Enrollment in the REVERSE trial, a phase 3 clinical study of GS010 (GenSight Biologics) in the treatment of patients with Leber's hereditary optic neuropathy (LHON) has been successfully completed. REVERSE is the first of

two parallel, randomized, double-blind, sham-controlled pivotal phase 3 studies designed to evaluate the efficacy of a single intravitreal injection of GS010 in subjects with LHON due to the G11778A mutation in the mitochondrial *ND4* gene. The study enrolled 36 patients with vision loss for seven to 12 months, whereas RESCUE, the second trial, is enrolling 36 patients with vision loss for less than six months. Both studies are being conducted in the United States and Europe.

Source: GenSight Biologics, February 21, 2017

Napabucasin for Pancreatic Cancer

Boston Biomedical has initiated treatment in the first patient enrolled in a global phase 3 study investigating napabucasin—an orally administered, first-in-class, investigational agent designed to inhibit cancer stemness pathways by targeting STAT3—in combination with standard of care (nab-paclitaxel plus gemcitabine) in patients with metastatic pancreatic cancer. A total of 1,132 patients who have not been treated with systemic chemotherapy or investigational agents will be enrolled in the study. The primary endpoint is overall survival.

Source: Boston Biomedical, February 21, 2017

Zuprata for Macular Edema

The first patient has been enrolled in a phase 3 trial of Zuprata (Clearside Biomedical), a suspension formulation of the corticosteroid triamcinolone acetonide, used with aflibercept (Eylea, Regeneron), for the treatment of macular edema associated with retinal vein occlusion (RVO).

The SAPPHIRE trial is a multicenter, randomized, masked, controlled study designed to assess the efficacy and safety of suprachoroidally administered Zuprata, used with intravitreally administered alibercept, compared with aflibercept alone in patients with RVO. After 24 weeks of treatment, patients will be followed for approximately six additional months.

Source: Clearside Biomedical, February 16, 2017

TRC105 for Angiosarcoma

Tracon Pharmaceuticals has initiated patient dosing in its phase 3 TAPPAS trial of TRC105. The study has an initial enrollment target of 124 patients, and the primary endpoint is progression-free survival. TRC105 is an antibody to endoglin, a protein overexpressed on proliferating endothelial cells that is essential for angiogenesis.

Source: Tracon Pharmaceuticals, February 16, 2017

DB102 for Lymphoma

Denovo Biopharma plans to initiate a biomarker-driven, phase 3 study of DB102 as a first-line therapy for patients with diffuse large B-cell lymphoma this year. The study will be conducted in the United States and China. DB102 (formerly known as enzastaurin) is an orally available, investigational small-molecule serine/threonine kinase inhibitor of the protein kinase C-beta and AKT pathways. It has been studied in more than 3,000 patients with solid or hematologic tumors.

Source: Denovo Biopharma, February 16, 2017

Bekinda for Gastroenteritis And Gastritis

The last patient has been enrolled in a phase 3 study of Bekinda (RedHill Biopharma)—an extended-release, once-daily oral formulation of the antiemetic drug ondansetron—in patients with acute gastroenteritis and gastritis. The randomized, double-blind, placebo-controlled GUARD trial is investigating Bekinda 24 mg in 320 children and adults (12 years of age and older). Top-line results are expected in the second quarter of 2017.

Source: RedHill Biopharma, February 13, 2017

DEVICE APPROVALS

MRIdian Linac Radiation Therapy System

ViewRay, Inc., has received 510(k) clearance from the FDA to market the MRIdian Linac system, a linear accelerator-based magnetic resonance imaging (MRI)-guided radiation therapy system. The first two systems in the United States are expected to be installed at Henry Ford Hospital in Detroit and at Barnes–Jewish Hospital at Washington University in St. Louis. MRIdian Linac is the world's first commercial system to combine MRI for soft-tissue visualization and a compact linear accelerator.

Source: ViewRay, February 27, 2017

Vidas Brahms PCT Assay for LRT Infections and Sepsis

The FDA has given the green light to expanded use of the Vidas Brahms PCT assay (bioMérieux, Inc.) to help health care providers determine whether antibiotic treatment should be started or stopped in patients with lower respiratory tract (LRT) infections, such as community-acquired pneumonia, and stopped in patients with sepsis. This is the first test to use procalcitonin (PCT), a protein associated with the body's response to a bacterial infection, as a biomarker to help make antibiotic management decisions in patients with these conditions. The test works by measuring PCT. High levels of PCT suggest a bacterial infection, whereas low levels suggest a viral infection or noninfectious causes.

Source: bioMérieux, February 24, 2017

TAP Blood-Collection Device

The FDA has awarded 510(k) clearance to a new blood-collection device called TAP (Seventh Sense Biosystems). The walnut-sized device attaches to the

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patient's arm with an adhesive strip and uses a ring of 30 spring-loaded microneedles to puncture the skin and withdraw 100 mcL of blood—enough for most blood tests. The TAP device can be used to collect capillary blood for hemoglobin A1c testing, which is routinely used to monitor blood sugar levels in diabetic or prediabetic patients. The product's manufacturer has described it as being "virtually painless."

Source: Seventh Sense Biosystems, February 23, 2017

SeptiCyte LAB Assay for Sepsis

Immunexpress, Inc., a molecular diagnostic company based in Seattle, has received 510(k) clearance from the FDA for the use of its SeptiCyte LAB assay as an aid in differentiating infection-positive (sepsis) from infection-negative (SIRS) systemic inflammation in critically ill patients on their first day of admission to the intensive care unit. It is the first RNA-based clinical diagnostic tool, direct from whole blood, to aid medical providers in the early identification of infection in suspected sepsis patients, according to the company. The technology quantifies specific molecular markers from the patient's immune system—the "host response"—rather than invading pathogens.

Source: Immunexpress, February 22, 2017

Coronary Stent System

The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System (Biotronik) has won FDA approval using results from the BIOHELIX-I clinical study. The stent, which has been used to treat more than 650,000 patients worldwide, is now available in the U.S. It is designed to improve the coronary luminal diameter in patients with new and reoccurring blockages in coronary arteries.

The prospective, nonrandomized BIOHELIX-I trial evaluated the stent system in 329 patients. At nine months, the target vessel failure rate was 9%—less than half of the performance goal of 19%.

Source: Biotronik, February 15, 2017 ■