NEW DRUG APPROVALS

Nuplazid for Parkinson's Psychosis

Pimavanserin (Nuplazid, Acadia Pharmaceuticals) has received FDA approval for the treatment of patients with hallucinations and delusions associated with Parkinson's disease psychosis. It is the first medication approved by the FDA for this indication.

Pimavanserin preferentially targets 5-HT_{2A} receptors, which are thought to play an important role in Parkinson's disease psychosis. The pharmacology of pimavanserin establishes a new class of drug—selective serotonin inverse agonists (SSIA)—by not only preferentially targeting 5-HT_{2A} receptors, but also by avoiding activity at dopamine and other receptors commonly targeted by antipsychotics.

Typical Parkinson's disease therapy consists of drugs that stimulate dopamine to treat patients' motor symptoms, such as tremor, muscle rigidity, and difficulty walking. Pimavanserin does not interfere with patients' dopaminergic therapy and therefore does not impair their motor function.

Source: Acadia Pharmaceuticals, April 29, 2016

Cabometyx for Renal Cell Carcinoma

The FDA has approved cabozantinib tablets (Cabometyx, Exelixis, Inc.) for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior antiangiogenic therapy. RCC is the most common form of kidney cancer in adults.

Cabozantinib, which was granted fast-track and breakthrough therapy designations by the FDA, is the first therapy to demonstrate clinically meaningful improvements in all three key efficacy parameters—overall survival, progression-free survival, and the objective response rate—in a phase 3 trial of patients with advanced RCC.

Cabozantinib targets include MET, AXL, and vascular endothelial growth factor receptor-1, -2, and -3. In preclinical models, cabozantinib inhibited the activity of these receptors, which are involved in normal cellular function as well as pathological processes, such as tumor angiogenesis, invasiveness, metastasis, and drug resistance.

Source: Exelixis, April 26, 2016

Xtampza ER for Severe Pain

Xtampza ER (oxycodone) extended-release (ER) capsules CII (Collegium Pharmaceutical, Inc.) have won full marketing approval from the FDA.

The drug was awarded tentative approval in November 2015, but full approval was contingent on the outcome of a lawsuit filed by Purdue Pharma against Collegium. Purdue, which has developed abuse-deterrent versions of OxyContin (oxycodone), claimed that Xtampza infringed on some of its patents. In February, however, the U.S. District Court of Massachusetts ruled in favor of Collegium.

Xtampza ER is an opioid agonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. It is designed to provide adequate pain control while maintaining its drug-release profile after being subjected to common methods of manipulation, including chewing and crushing the product before administration.

Source: Collegium Pharmaceutical, April 26, 2016

Orfadin for Hereditary Tyrosinemia

The FDA has approved nitisinone oral suspension (Orfadin, Swedish Orphan Biovitrum) for the treatment of hereditary tyrosinemia type-1 (HT-1) in combination with dietary restriction of tyrosine and phenylanine. HT-1 is a rare genetic disease that affects infants and children. It is progressive and may result in liver and kidney complications that can be fatal if untreated. Nitisinone blocks the breakdown of tyrosine.

Source: Swedish Orphan Biovitrum, April 26, 2016

Triferic Powder for Anemia In Hemodialysis Patients

Triferic powder packet (Rockwell Medical) has won FDA approval for commercial sale as an iron-replacement product to maintain hemoglobin in adult patients with hemodialysis-dependent chronic kidney disease. Triferic is delivered to hemodialysis patients via dialysate, replacing the ongoing iron loss that occurs during their dialysis treatment. It is added to the bicarbonate concentrate on-site at the dialysis clinic.

Source: Rockwell Medical, April 26, 2016

Bevespi Aerosphere for COPD

The FDA has given the green light to Bevespi Aerosphere inhalation aerosol (glycopyrrolate and formoterol fumarate, AstraZeneca) for the long-term maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease, including chronic bronchitis and/or emphysema. It is the only long-acting dual bronchodilator delivered through a pressurized metered-dose inhaler.

Bevespi Aerosphere is a twice-daily, fixed-dose dual bronchodilator combining glycopyrrolate, a long-acting muscarinic antagonist, and formoterol fumarate, a long-acting beta-2 agonist.

Source: AstraZeneca, April 25, 2016

Generic Approvals

Rosuvastatin Calcium

The FDA has approved the first generic version of AstraZeneca's Crestor, which had U.S. sales of approximately $6.5 billion for the 12 months ending with March 2016.

Rosuvastatin calcium tablets are approved for the following uses: 1) in combination with diet for the treatment of hypertriglyceridemia in adults; 2) in combination with diet for the treatment of patients with primary dysbetalipoproteinemia (type III hyperlipoproteinemia), a disorder associated with the improper breakdown of cholesterol and triglycerides; and 3) either alone or in combination with other cholesterol treatments for adult patients with homozygous familial hypercholesterolemia, a disorder associated with high low-density lipoprotein-cholesterol.

Actavis Inc. (a subsidiary of Allergan) has received approval to market generic rosuvastatin calcium in multiple strengths. Under terms of an agreement reached with AstraZeneca in 2013, Allergan launched its generic version of Crestor 67 days prior to July 8, 2016, the expiration of exclusivity. Allergan predicted that this will be the largest generic launch of 2016.

Sources: FDA, April 29, 2016, and Allergan, May 2, 2016

Glyburide

Zydus Cadila Healthcare has received final approval from the FDA to market glyburide tablets USP in strengths of 1.25 mg, 2.5 mg, and 5.0 mg. Glyburide, an antidiabetes drug, will be produced at the company's manufacturing facility in India.

Source: Zydus Cadila Healthcare, May 11, 2016

Sodium Phenylbutyrate

Par Formulations has secured FDA approval for sodium phenylbutyrate 500-mg tablets, a generic equivalent of Buphenyl tablets (Horizon Pharma).

Sodium phenylbutyrate is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase, ornithine transcarbamylase, or argininosuccinic acid synthetase. It is indicated for all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated for patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. The drug must be combined with dietary protein restriction and, in some cases, essential amino acid supplementation.

Source: FDA, May 11, 2016

Estradiol Valerate and Estradiol Valerate/Dienogest

Allergan has received FDA approval for the marketing of estradiol valerate 1-mg and 3-mg tablets and estradiol valerate/dienogest 2-mg/2-mg and 2-mg/3-mg tablets, which are blister-packed together in the order in which they should be taken. The drug is a generic version of the birth-control product Natazia (Bayer HealthCare) and is also indicated to alleviate heavy menstrual bleeding.

Source: FDA, May 6, 2016

Diclofenac Potassium for Oral Solution

The FDA has granted approval to diclofenac potassium for oral solution, 50 mg (Par Formulations). Diclofenac potassium is a nonsteroidal anti-inflammatory drug indicated for the treatment of migraine attacks with or without aura in adults 18 years of age or older. The drug, which is manufactured as a soluble powder, is mixed with water and taken orally. This is the first generic version of the oral formulation, which was approved by the FDA as Cambia (Depomed, Inc.).

Source: FDA, May 2, 2016

Lacosamide

Seven manufacturers have earned FDA approval to produce generic versions of lacosamide. One approval was granted for a 10-mg/mL oral solution (Amneal Pharmaceuticals) and six approvals were granted for the marketing of tablets in 50-, 100-, 150-, and 200-mg strengths (Actavis Laboratories, MSN Laboratories, Alembic Pharmaceuticals, Aurobindo Pharma, Mylan Pharmaceuticals, and Sun Pharmaceutical Industries). Lacosamide is indicated for the treatment of partial-onset seizures in patients 17 years of age or older. The drug was first approved as Vimpat (UCB, Inc.) in 2008.

Source: FDA, April 28, 2016

Fosamprenavir Calcium

Mylan Pharmaceuticals has received FDA approval for the first generic 700-mg tablet version of Lexiva (fosamprenavir calcium, ViiV Healthcare). Fosamprenavir calcium is a human immunodeficiency virus (HIV) protease inhibitor indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adult and pediatric patients.

Source: FDA, April 15, 2016

Flurandrenolide Cream USP, 0.05%

The FDA has allowed Teligent, Inc., to market flurandrenolide cream USP, 0.05%. The topical drug is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. This is a generic version of Cordran cream (Aqua Pharmaceuticals), which was approved in 1965.

Source: FDA, April 13, 2016

Rosiglitazone Maleate/Glimepiride Combination Tablet

Teva Pharmaceuticals USA has received FDA approval for the manufacture of rosiglitazone maleate/glimepiride tablets in 1-mg/4-mg, 2-mg/4-mg, 4-mg/4-mg, 2-mg/8-mg, and 4-mg/8-mg dosages. Originally approved as Avandaryl (GlaxoSmithKline), rosiglitazone maleate/glimepiride is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes when treatment with both rosiglitazone and glimepiride is appropriate. It should not be used in patients with type-1 diabetes or for the treatment of diabetic ketoacidosis.

Source: FDA, April 1, 2016

Frovatriptan Succinate

Mylan has announced the U.S. launch of frovatriptan succinate tablets 2.5 mg, a generic version of Frova (Endo Pharmaceuticals), which is used to treat acute migraine headaches in adults.

Source: Mylan, May 12, 2016

NEW INDICATIONS

Imbruvica for SLL

The FDA has approved an expansion to the prescribing information for ibrutinib (Imbruvica, Janssen/AbbVie) based on data supporting its use in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

The approved label now includes overall survival (OS) data from the phase 3 RESONATE-2 trial in treatment-naïve CLL/SLL patients 65 years of age or older. The updated label also contains clinical data from the phase 3 HELIOS trial, which investigated the use of ibrutinib in combination with bendamustine and rituximab (BR) compared with placebo plus BR in patients with relapsed or refractory CLL/SLL.

Ibrutinib was approved in March 2016 as a first-line treatment for patients with CLL. After reviewing the new phase 3 data, the FDA decided to expand the drug's CLL indication to include the treatment of SLL patients with or without deletion of the chromosome 17p. SLL is a slow-growing lymphoma that is similar to CLL.

Source: Janssen, May 10, 2016

Viekira Pak for HCV In Cirrhosis Patients

The FDA has approved a supplemental new drug application for the use of Viekira Pak (ombitasvir, paritaprevir, and ritonavir tablets with dasabuvir tablets) without ribavirin in patients with genotype 1b chronic hepatitis C virus (HCV) infection and compensated cirrhosis (Child–Pugh class A). The application was previously granted a priority review.

Ombitasvir is an HCV NS5A inhibitor; paritaprevir is an HCV NS3/4A protease inhibitor; ritonavir is a cytochrome P450-3A inhibitor; and dasabuvir is an HCV non-nucleoside NS5B palm polymerase inhibitor.

Viekira Pak is used with or without ribavirin to treat adults with genotype 1 chronic HCV infection and can now be used in patients with compensated cirrhosis. The treatment is not intended for patients with advanced (decompensated) cirrhosis.

Source: AbbVie, April 25, 2016

FDA REVIEW ACTIVITIES

Priority Review Status

Olaratumab for Soft Tissue Sarcoma

The FDA has granted priority review to a biologics license application for olaratumab (Eli Lilly and Company) in combination with doxorubicin for the potential treatment of patients with advanced soft tissue sarcoma (STS) that is not amenable to curative treatment with radiotherapy or surgery. Olaratumab previously received FDA breakthrough therapy, fast-track, and orphan drug designations for this indication.

Olaratumab is a human immunoglobulin G1 monoclonal antibody that is designed to disrupt the platelet-derived growth factor receptor-alpha pathway on tumor cells and on cells in the tumor microenvironment. This means that it may induce anticancer activity by targeting tumor cells directly, as well as cells that surround and support tumor growth. A phase 3 trial of olaratumab and doxorubicin in advanced STS is currently recruiting adult patients.

Source: Eli Lilly, May 4, 2016

Fast-Track Designation

RecAP for Acute Kidney Injury

AM-Pharma announced that it has received a fast-track designation from the FDA for recAP (recombinant human alkaline phosphatase) to treat patients with acute kidney injury (AKI). The company is conducting a phase 2 study of recAP in at least 290 patients with AKI in North America and Europe.

Source: AM-Pharma, April 26, 2016

Breakthrough Therapy Status

Ilaris for Periodic Fever Syndromes

The FDA has granted three breakthrough therapy designations for canakinumab (Ilaris, Novartis) to treat three rare types of periodic fever syndrome, also known as hereditary periodic fevers.

Canakinumab is a selective, high-affinity, human monoclonal antibody that inhibits interleukin-1 (IL-1) beta, an important part of the body's immune defenses. Excessive production of IL-1 beta plays a prominent role in certain inflammatory diseases. Canakinumab works by blocking the action of IL-1 beta for a sustained period, thereby inhibiting the inflammation that is caused by its overproduction.

The three conditions for which Ilaris is being reviewed are tumor necrosis factor-receptor-associated periodic syndrome;

hyperimmunoglobulin D syndrome/mevalonate kinase deficiency; and familial Mediterranean fever not adequately controlled with colchicine.

The FDA approved Ilaris in 2009 to treat two subtypes of a rare autoinflammatory disease called cryopyrin-associated periodic syndromes—Muckle–Wells syndrome and familial cold autoinflammatory syndrome—in patients 4 years of age and older. In 2013, the FDA approved Ilaris for a rare, autoinflammatory form of juvenile idiopathic arthritis called systemic juvenile idiopathic arthritis in patients 2 years of age and older.

Source: Novartis, April 27, 2016

Orphan Drug Designations

Selumetinib for Thyroid Cancer

Selumetinib (AstraZeneca), an investigational MEK 1/2 inhibitor, has received orphan drug status from the FDA for the adjuvant treatment of patients with stage III or IV differentiated thyroid cancer (DTC). In July 2015, selumetinib failed to meet its goal in a late-stage trial for uveal melanoma, a rare eye cancer.

An ongoing phase 3, double-blind, randomized trial is comparing complete remission rates after a five-week course of selumetinib or placebo plus single-dose adjuvant radioactive iodine (RAI) therapy in patients with DTC who are at high risk of recurrence. In a phase 2 study of selumetinib in patients with advanced thyroid cancer, clinically meaningful increases in iodine uptake and retention were seen in patients with disease that was refractory to RAI.

Sources: AstraZeneca and Reuters, May 12, 2016

VAL-083 for Ovarian Cancer

The FDA has granted orphan drug status to VAL-083 (DelMar Pharmaceuticals), a first-in-class small-molecule chemotherapeutic, for the treatment of ovarian cancer. VAL-083 previously received an orphan drug designation for glioma and medulloblastoma.

In more than 40 phase 1 and phase 2 clinical studies sponsored by the National Cancer Institute, VAL-083 demonstrated clinical activity against a range of malignancies, including lung, brain, cervical, and ovarian cancers and leukemia, both as a single agent and in combination with other treatments.

Source: DelMar Pharmaceuticals, April 21, 2016

Complete Response Letters

Mycapssa for Acromegaly

Executives at Chiasma, a Massachusetts-based biopharmaceutical company, plan to challenge the FDA over its rejection of the company's new drug application (NDA) for octreotide (Mycapssa), an oral maintenance treatment for adults with acromegaly.

In April, the FDA sent Chiasma a complete response letter stating that the company's application had not provided sufficient evidence of efficacy to warrant approval. The FDA expressed concern about certain aspects of the company's single-arm, open-label, phase 3 clinical studies. The agency requested that Chiasma conduct a randomized, double-blind, controlled trial that enrolls patients in the United States and that is of sufficient duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment.

During a conference call in May, a Chiasma executive said the company disagrees with the FDA's decision, asserting that information included in the NDA "demonstrates the efficacy and safety of Mycapssa." Chiasma's leadership was making plans to meet with FDA representatives by the end of June to present their case.

Source: *Boston Business Journal*, May 12, 2016

Abilify/Ingestible Sensor Combo

The FDA has issued a complete response letter for Digital Medicine (Otsuka Pharmaceutical/Proteus Digital Health), a drug/device product that combines the atypical antipsychotic aripiprazole (Abilify, Otsuka) with the FDA-cleared Proteus ingestible sensor embedded in a single tablet at the point of manufacture.

In the new drug application submitted by Otsuka and Proteus, the product was described as a system that measures medication adherence to aripiprazole as a treatment for schizophrenia, as an acute treatment of manic and mixed episodes associated with bipolar 1 disorder, and as an adjunctive treatment for major depressive disorder.

After completing its review, the FDA requested additional clinical information, including data regarding the performance of the product under the conditions in which it is likely to be used, and further human-factors investigations. The goal of human-factors testing is to evaluate use-related risks and to confirm that patients can use the device safely and effectively.

Source: Otsuka, April 26, 2016

Revised Application

IV Carbamazepine for Epilepsy

The FDA has accepted for review the resubmission of a new drug application for Carnexiv (Lundbeck), an intravenous (IV) formulation of the antiepileptic drug carbamazepine. An action letter is anticipated before the end of 2016.

The resubmission was in reply to a complete response letter from the FDA issued in 2014 requesting additional data regarding the chemistry, manufacturing, and controls of the product. The proposed U.S. trade name, Carnexiv, is under consideration by the FDA as well.

IV carbamazepine received an orphan drug designation from the FDA in 2013 and is proposed for use as replacement

therapy in adults who are receiving a stable maintenance oral dose of carbamazepine to control certain seizure types when oral carbamazepine administration is temporarily not feasible.

Source: Lundbeck, April 22, 2016

DRUG SAFETY ISSUES

Dementia in AF Patients Receiving Warfarin

A study of 10,537 patients receiving long-term treatment with the blood thinner warfarin has revealed higher rates of dementia in patients with atrial fibrillation (AF) compared with those without that common heart-rhythm disorder.

During a follow-up period of approximately seven years, researchers at the Intermountain Medical Center Heart Institute found that all types of dementia increased in the AF group more than in the non-AF group. In both cohorts, however, the risk of dementia increased as the time in therapeutic range decreased or became more erratic. When warfarin levels were consistently too high or too low, dementia rates increased regardless of why patients were receiving a blood thinner. The findings were presented at the 37th Annual Scientific Sessions of the Heart Rhythm Society in San Francisco.

Source: Intermountain Health, May 5, 2016

Compulsive Urges With Aripiprazole

The FDA has warned that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the antipsychotic drug aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). These uncontrollable urges were reported to have stopped when the medication was discontinued or the dose was reduced. These impulse-control problems are rare, the agency says, but they may result in harm to the patient and others if not recognized.

Aripiprazole is used to treat schizophrenia, bipolar disorder, Tourette's disorder, and irritability associated with autistic disorder. It may also be used in combination with antidepressants to treat depression.

Source: FDA, May 3, 2016

Fluconazole and Miscarriage

The FDA is evaluating the results of a Danish study that concluded there is a possible increased risk of miscarriage with the use of oral fluconazole (Diflucan, Pfizer, and generics) for the treatment of yeast infections. Most of the oral fluconazole use in this study appeared to be one or two doses of 150 mg. In 2011, the FDA issued a safety communication stating that long-term use of high-dose fluconazole (400 to 800 mg per day) during pregnancy may be associated with birth defects in infants.

Source: FDA, April 26, 2016

CLINICAL TRIAL NEWS

Algenpantucel-L Flops in Pancreatic Cancer Trial

Algenpantucel-L (NewLink Genetics Corporation) did not improve survival among patients with resected pancreatic cancer in the phase 3, randomized, controlled IMPRESS trial.

Patients received algenpantucel-L in combination with the standard of care compared with standard of care alone. A total of 722 patients with surgically removed cancers were enrolled in the United States from May 2010 to September 2013.

The study did not achieve its primary endpoint. Overall survival from the time of randomization was 29.3 months for both treatment groups combined. There was no statistically significant difference between the two groups. Median survival was 30.4 months and 27.3 months for the control and study groups, respectively.

There was also no statistical difference for long-term survival. Three-year survival was 41.4% and 42.1% and four-year survival was 32.6% and 32.7% for the control and study groups, respectively.

Source: NewLink Genetics, May 11, 2016

Baxdela Effective for Skin And Skin-Structure Infections

Positive results have been reported from a phase 3, randomized, double-blind study of delafloxacin (Baxdela, Melinta Therapeutics), an investigational anionic quinolone in development for the treatment of patients with acute bacterial skin and skin-structure infections.

Intravenous (IV)-to-oral monotherapy with delafloxacin was compared with the standard-of-care IV-only combination of vancomycin and aztreonam.

In the intent-to-treat (ITT) population, IV-to-oral delafloxacin achieved the primary endpoint of statistical noninferiority in the early clinical response at 48 to 72 hours after initiation of therapy (83.7%) compared with IV combination therapy with vancomycin and aztreonam (80.6%).

Delafloxacin also met the endpoint of statistical noninferiority (57.7%) compared with vancomycin plus aztreonam (59.7%) based on the investigators' assessment of a complete cure (i.e., the resolution of all baseline signs and symptoms) at the follow-up visit in the ITT population. Further, delafloxacin was comparable with vancomycin plus aztreonam in achieving treatment success at follow-up (i.e., cured or improved, with no further antibiotics needed), with a success rate of 87.2% versus 84.8%, respectively.

Source: Melinta Therapeutics, May 12, 2016

Vivlodex Relieves OA Pain

New phase 3 data have demonstrated that patients with osteoarthritis (OA) pain treated with 5 mg or 10 mg of Vivlodex (meloxicam capsules, Iroko Pharmaceu-

ticals) used significantly less total rescue medication and took fewer daily doses of rescue medication for fewer days compared with patients receiving placebo. The greatest benefits were seen in patients given the 10-mg dose. Regardless of the time of day, patients receiving Vivlodex 10 mg per day required approximately half as many rescue pain medication doses as did patients receiving placebo.

The double-blind study involved 403 patients with OA of the knee or hip who were chronic users of nonsteroidal anti-inflammatory drugs (NSAIDs) and/or acetaminophen. The patients were randomly assigned to receive either 5 mg or 10 mg of Vivlodex once daily or placebo for 12 weeks. Rescue medication (acetaminophen 500 mg every four to six hours) was permitted.

Source: Iroko Pharmaceuticals, May 12, 2016

Adenovirus Vaccine Aids Colon Cancer Survival

A genetically engineered adenovirus vaccine designed to treat patients with colon cancer more than doubled the survival rate, with little or no toxicity, in subjects with end-stage disease—with some subjects still alive more than five years after receiving only the vaccine.

The new phase 2 data were presented by Patrick Soong-Shiong, MD, at the Bank of America Merrill Lynch 2016 Health Care Conference in Las Vegas, Nevada. Dr. Soon-Shiong is the inventor of the first human nanoparticle chemotherapeutic agent, paclitaxel (Abraxane, Celgene Corporation).

Dr. Soon-Shiong told attendees that the vaccine, a genetically engineered common cold virus (adenovirus) that displays the unique biological signature of the patient's carcinoembryonic antigen, is injected subcutaneously like a flu shot. The vaccine directs dendritic cells to activate killer T cells, thus programming the patient's immune system to develop lifelong immunity against cancer cells. In the new trial, treatment with the vaccine more than doubled median survival in patients who had failed all standard forms of therapy and had an expected historical survival rate of less than 4.5 months.

Source: NantWorks, May 10, 2016

DRM01 Improves Facial Acne Vulgaris

Positive results have been reported from a phase 2b dose-ranging study of DRM01 (Dermira, Inc.) in patients with facial acne vulgaris. DRM01 is an investigational small molecule designed to inhibit sebum production after topical application.

Subjects were instructed to apply DRM01 at concentrations of 4.0% once daily (n = 106), 7.5% once daily (n = 110), or 7.5% twice daily (n = 101), or to apply vehicle once or twice daily (n = 53 and n = 50, respectively), in all cases for 12 weeks. The number of inflammatory lesions in patients treated with the highest dose of DRM01 was reduced by an average of 15.0 compared with 10.7 among the patients in the combined vehicle group ($P = 0.001$), for an average percentage reduction of 55.6% compared with 40.0%, respectively ($P < 0.001$).

After 12 weeks of treatment, 25.9% of patients receiving the highest dose of DRM01 achieved at lease a two-grade improvement in the Investigator's Global Assessment score compared with 9.8% of the patients in the combined vehicle group ($P = 0.004$).

Source: Dermira, Inc., May 10, 2016

Ulipristal Acetate Lessens Uterine Fibroid Bleeding

Allergan and Gedeon Richter have announced positive results from a pivotal, phase 3 trial evaluating the efficacy and safety of ulipristal acetate in women with uterine fibroids.

A total of 157 patients were randomly assigned to receive ulipristal acetate (5 mg or 10 mg; n = 101) or placebo (n = 56). Significantly more patients in the ulipristal 5-mg group (47.2%; $P < 0.0001$) and in the ulipristal 10-mg group (58.3%; $P < 0.0001$) achieved an absence of uterine bleeding compared with placebo (1.8%). The most common adverse events associated with ulipristal included hypertension, increased blood creatine phosphokinase, hot flush, and acne.

Source: Allergan, May 9, 2016

Fasinumab Reduces OA Pain

Regeneron Pharmaceuticals announced positive results from a phase 2/3, placebo-controlled study evaluating fasinumab, an investigational nerve growth factor (NGF) antibody, in 421 adults with moderate-to-severe osteoarthritis pain of the hip or knee and a history of inadequate pain relief or intolerance to current analgesic therapies. After 16 weeks of treatment, patients treated with 1 mg, 3 mg, 6 mg, or 9 mg of fasinumab demonstrated statistically significant improvements in pain relief (the study's primary endpoint), as well as improvements in physical functioning, compared with placebo.

As expected with an antibody to NGF, the fasinumab dosing groups showed an increase in certain neuromusculoskeletal adverse events compared with placebo (17% versus 6%, respectively). These events included arthralgia, paresthesia, hypoesthesia, and peripheral edema.

Source: Regeneron Pharmaceuticals, May 2, 2016

Ninlaro Lengthens PFS In Multiple Myeloma

Positive results have been reported from an international, phase 3, randomized, double-blind, placebo-controlled study evaluating once-weekly ixazomib capsules (Ninlaro, Takeda Pharmaceu-

tical Company) plus lenalidomide and dexamethasone compared with placebo plus lenalidomide and dexamethasone in patients with relapsed and/or refractory multiple myeloma. The findings were published in the *New England Journal of Medicine*.

The TOURMALINE-MM1 trial, which included 722 patients with multiple myeloma, was the first phase 3 study of an oral proteasome inhibitor. The trial results demonstrated a statistically significant 35% extension of progression-free survival (PFS) with ixazomib in combination with lenalidomide and dexamethasone compared with the control group (median PFS: 20.6 months versus 14.7 months, respectively; $P = 0.01$) after a median follow-up period of 14.7 months. The overall response rates were 78% in the ixazomib arm and 72% in the placebo arm.

Source: Takeda, April 27, 2016

Paclical Noninferior For Ovarian Cancer

Oasmia Pharmaceutical has announced positive overall survival (OS) results from a phase 3 study of Paclical (also known as Apealea), a water-soluble formulation of paclitaxel, in 789 women with epithelial ovarian cancer.

The preliminary results demonstrated noninferiority between the two treatment groups: Paclical in combination with carboplatin versus Taxol (paclitaxel, Bristol-Myers Squibb) in combination with carboplatin. OS in patients completing six treatment cycles was 25.7 months in those treated with the Paclical combination compared with 24.8 months in those treated with the Taxol combination. The new data will form the basis of a marketing application to the FDA.

Source: Oasmia Pharmaceutical, April 27, 2016

Biotin Stops Progress Of Multiple Sclerosis

Encouraging data were reported from the MS-SPI trial, which tested the efficacy of MD1003 (MedDay Pharmaceuticals), a pharmaceutical-grade biotin, in patients with "not active" progressive multiple sclerosis (MS), for which there is no approved treatment.

Patients were randomly assigned to receive either MD1003 (n = 103) or placebo (n = 51) for 12 months, followed by a 12-month extension phase during which all patients received MD1003. The study's primary endpoint was the proportion of patients demonstrating reversal of disability after nine months of treatment (M9), confirmed at 12 months (M12).

The study's primary endpoint was met, with 13% of the patients in the MD1003 arm showing confirmed reversal of progression at M9 (confirmed at M12), compared with none of the patients in the placebo arm ($P = 0.0051$). During the 12-month extension phase, patients initially treated with MD1003 exhibited sustained improvement versus baseline, with 13% of patients showing improvement at M18 (confirmed at M24) and 15% of patients showing improvement at M24.

Source: MedDay Pharmaceuticals, April 21, 2016

Edaravone Helpful in ALS

A phase 3 study of edaravone (MCI-186, Mitsubishi Tanabe Pharma Corporation) in subjects with amyotrophic lateral sclerosis (ALS) met its primary efficacy endpoint of a change in the ALS Functional Rating Scale–Revised at 24 weeks.

Edaravone has been studied in Japan for the treatment of ALS but has not been investigated in the U.S. It is believed to relieve the effects of oxidative stress—a key factor in the onset and progression of ALS. Patients with ALS show consistent increases in oxidative stress biomarkers.

The frequency of adverse events was similar for edaravone and placebo.

Source: Mitsubishi Tanabe Pharma Corporation, April 20, 2016

Ibrance for Breast Cancer

A phase 3 trial of palbociclib (Ibrance, Pfizer) met its primary endpoint by demonstrating an improvement in progression-free survival with the combination of palbociclib and letrozole compared with letrozole plus placebo in postmenopausal women with estrogen receptor–positive, human epidermal growth factor receptor 2–negative advanced or metastatic breast cancer who had not received previous systemic treatment for their advanced disease.

The new data will support a request for conversion of the accelerated approval for palbociclib to regular approval in the United States. Palbociclib is an oral, first-in-class inhibitor of cyclin-dependent kinases 4 and 6.

Source: Pfizer, April 19, 2016

Deflazacort for Muscular Dystrophy

Positive results have been reported from a pivotal phase 3 study of deflazacort (Marathon Pharmaceuticals), an investigational glucocorticoid with anti-inflammatory and immunosuppressant properties, in patients with Duchenne muscular dystrophy (DMD).

A randomized, double-blind, placebo-controlled, active-comparator study randomly assigned 196 patients with DMD to receive deflazacort 0.9 mg/kg per day, deflazacort 1.2 mg/kg per day, prednisone 0.75 mg/kg per day, or placebo for 12 weeks. The study's primary endpoint was the change in average muscle strength from baseline to week 12 with deflazacort or prednisone compared with placebo. Deflazacort met the study's primary endpoint compared with placebo ($P = 0.0173$ and $P = 0.0003$ for the

0.9 mg/kg and 1.2 mg/kg daily doses, respectively).

Source: Marathon Pharmaceuticals, April 19, 2016

Opdivo Extends OS in Head-and-Neck Cancer

A phase 3, open-label, randomized study evaluated nivolumab (Opdivo, Bristol-Myers Squibb) in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck after platinum therapy compared with the investigator's choice of therapy (methotrexate, docetaxel, or cetuximab).

The trial was stopped early after an independent data monitoring committee concluded that the study had met its primary endpoint of overall survival (OS) in patients receiving nivolumab compared with the control arm. Patients treated with nivolumab experienced a 30% reduction in the risk of death, with median OS of 7.5 months compared with 5.1 months for the investigator's choice of therapy (hazard ratio, 0.70; $P = 0.0101$). The one-year survival rate for nivolumab was 36% compared with 17% for the control arm.

Source: Bristol-Myers Squibb, April 19, 2016

Bococizumab for CVD

Patient enrollment is complete in the global SPIRE-2 cardiovascular outcomes study of investigational bococizumab (Pfizer). SPIRE-2 is evaluating the efficacy and safety of bococizumab compared with placebo in reducing the risk of major cardiovascular events among approximately 10,600 patients at high risk for cardiovascular disease (CVD)—including those without a history of cardiovascular events—who are receiving effective statins or have documented statin intolerance.

Bococizumab is a PCSK9 inhibitor being studied for its potential to reduce levels of low-density lipoprotein-cholesterol and improve cardiovascular outcomes in high-risk primary- and secondary-prevention patients.

Source: Pfizer, April 26, 2016

AC-1204 for Alzheimer's

Accera, Inc., has completed enrollment in a phase 3 study of AC-1204, a ketosis-inducing compound for the treatment of patients with mild-to-moderate Alzheimer's disease (AD). Accera expects to report top-line data in December 2016. The NOURISH AD trial is a 26-week, double-blind, randomized, placebo-controlled, parallel-group study investigating the effects of daily use of AC-1204 in subjects with mild-to-moderate AD, with an optional 26-week open-label extension. Endpoints will examine the effects of AC-1204 on memory, cognition, and global function among noncarriers of the epsilon 4 variant of the apolipoprotein E (*APOE4*) gene.

Source: Accera, May 12, 2016

Adempas Study Ended

Based on the recommendation of an independent data monitoring committee (DMC), Bayer has terminated a phase 2 study investigating riociguat (Adempas), a stimulator of soluable guanylate cyclase, in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias. The DMC observed that patients receiving riociguat were at a possible increased risk for death and other serious adverse events compared with patients in the placebo group. The DMC did not identify a specific cause or common feature among the patients who died, except that many appeared to have more-serious and more-advanced underlying lung disease compared with the study population as a whole.

Riociguat is indicated for the treatment of adults with persistent or recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and World Health Organization (WHO) functional class. The drug is also indicated for the treatment of adults with pulmonary arterial hypertension to improve exercise capacity and WHO functional class, and to delay clinical worsening.

Source: Bayer, May 12, 2016

DEVICE NEWS

Single-Drop Blood Test For Ovarian Cancer

Using metabolomics technology, the Canadian company Phenomenome Discoveries, Inc., found that specific metabolic abnormalities are present in the blood of women with ovarian cancer. The company has subsequently developed a test (OvAware) that can be performed on a single drop of blood.

The test has now been verified in two clinical studies—one in Japan (99 controls and 112 ovarian cancer patients) and one in Canada (1,041 controls and 325 ovarian cancer patients). In both studies, the blood test was able to detect ovarian cancer with 97% accuracy. The test is expected to be available in 2017.

Source: Phenomenome Discoveries, Inc., May 12, 2016

Lungpacer Diaphragm Pacing System Advances

Lungpacer Medical, Inc., has received the FDA's expedited access pathway (EAP) designation for the Lungpacer diaphragm pacing system, meant to treat patients who have been unable to wean from mechanical ventilation. The EAP is a new FDA program aimed at facilitating more-rapid patient access to breakthrough technologies.

The Lungpacer system is designed to activate the diaphragm using a temporary, minimally invasive, transvascular nerve stimulation approach that is expected to restore diaphragm strength and endurance in patients who have failed to wean from mechanical ventilation after

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their diaphragm muscle atrophied as a consequence of ventilator-induced diaphragm dysfunction. The Lungpacer system is an investigational device and is not for sale in any country.

Source: Lungpacer Medical, May 12, 2016

Exenatide Subdermal Pump

Intarcia Therapeutics has announced positive results from its FREEDOM-CVO trial, which evaluated the cardiovascular safety of ITCA 650, a matchstick-size, subdermal osmotic pump that delivers exenatide for the continuous control of type-2 diabetes. The study evaluated the safety of ITCA 650 (60 mcg per day) in approximately 4,000 patients receiving standard-of-care antidiabetes therapies. The average treatment duration was 1.2 years. The trial met its primary and secondary endpoints, providing the clinical data needed for a regulatory filing.

Exenatide is a glucagon-like peptide-1 (GLP-1) receptor agonist marketed globally as twice-daily and once-weekly self-injection therapies for patients with type-2 diabetes. If approved by the FDA, ITCA 650 would be the first injection-free GLP-1 product that can provide up to one year of medication from a single placement of the osmotic minipump.

Source: Intarcia Therapeutics, May 6, 2016

Four Million Catheters Recalled

Cook Medical has recalled more than four million catheters with Beacon Tip technology that have been found to exhibit polymer degradation of the catheter tip, resulting in tip fracture, separation, or both. The problem has resulted in 30 medical device reports to date.

Potential adverse events that may occur as a result of catheter polymer degradation include loss of device function, separation of a device segment leading to medical intervention, or complications resulting from a separated segment. Such complications include device fragments in the vascular system, genitourinary system, or other soft tissues. Fragments within the vascular system could result in embolization to the heart or lungs, or occluding blood flow to end organs.

Source: FDA, May 3, 2016 ■