PIPELINE REPORT
Second Quarter 2014

Information on recently approved, soon-to-be-approved and phase III trial specialty medications

The Walgreens Pipeline Report provides a summary of the specialty medications that may be approved by the FDA within the next few years. While not all-inclusive, this report focuses on medications in phase III studies that may impact treatment for certain specialty disease states or conditions. It also highlights select, recently approved or soon-to-be-approved specialty medications of interest to the marketplace. Drug information for approved products should be reviewed using the PI (prescribing information). For full PI, please refer to the DailyMed website. The medications with an asterisk indicate they have a boxed warning.

Note: This report is not intended for use by patients.

Medications to watch

Here is a closer look at a few recently approved or soon-to-be approved medications that may have a significant impact on therapeutic classes and treatment for specific disease states and conditions.

Cerdelga (eliglustat)

Genzyme has filed a new drug application (NDA) for Cerdelga (eliglustat) in the treatment of adult patients with Gaucher disease type 1. Cerdelga is an orally administered glucosylceramide synthase inhibitor that reduces the production of glucosylceramide. Symptoms of Gaucher disease are caused by the accumulation of glucosylceramide, a type of lipid, in cells and tissues leading to abnormal blood counts, enlarged liver or spleen, and destructive bone disease. The NDA filing was based on two phase III trials, ENGAGE and ENCORE.

Forty treatment-naïve patients with Gaucher disease type 1 were enrolled in ENGAGE and randomized to Cerdelga twice daily or to placebo. The primary endpoint of the trial was the percent change in spleen volume from baseline to 39 weeks of treatment. Spleen volume in patients treated with Cerdelga decreased from baseline by a mean of 28 percent compared with a mean increase of two percent in placebo patients, for an absolute difference of 30 percent. At the end of the trial, patients who received placebo were switched to treatment with Cerdelga. The most common side effects reported in this trial were headache, joint pain and diarrhea.

ENCORE was a randomized, controlled, open-label trial designed to determine whether Cerdelga is noninferior to Cerezyme (imiglucerase for injection). In the trial, 160 patients who had been receiving enzyme replacement therapy for at least three years and reached therapeutic goals were randomized (2:1) to receive either Cerdelga or Cerezyme for one year. The primary endpoint of the trial was disease stability, which included measurements of spleen volume, hemoglobin levels, platelet counts and liver volume. Cerdelga was found to be noninferior to Cerezyme, with the majority of patients in both groups remaining stable one year after randomization (84 percent in the Cerdelga group and 94 percent in the Cerezyme group).

Cerdelga is designated as an orphan drug. The FDA accepted the NDA filing and granted priority review status to the application in December 2013.

Siltuximab

Janssen has developed siltuximab for the treatment of multicentric Castleman disease (MCD) in patients who are HIV-negative and human herpes virus 8-negative. MCD is a rare disorder of the lymph nodes and related tissues. Clinical manifestations of MCD include serious infections, fevers, weight loss, fatigue, night sweats, nerve damage and anemia. MCD may be caused by the overproduction of interleukin-6 (IL-6). Siltuximab is an IL-6 inhibitor.

In a phase II, randomized, double-blind, placebo-controlled trial, 79 patients were randomized to receive either siltuximab 11 mg per kg (53 patients) or placebo (26 patients) administered by a one-hour intravenous (IV) infusion every three weeks. Patients in both groups also received best supportive care (BSC) to manage MCD symptoms. The primary endpoint of the trial was the number of patients who achieved a tumor and symptomatic response. Thirty-four percent of patients in the siltuximab group and none of the patients in the placebo group achieved the primary endpoint.

Siltuximab is designated as an orphan drug. Janssen filed a biologics license application (BLA) in September 2013, and the FDA granted priority review status to the application. A response to the BLA is expected in May 2014.

Ledipasvir

Ledipasvir is an investigational medication developed by Gilead Sciences for the treatment of genotype 1 chronic hepatitis C virus (HCV) infection. The phase III program consisted of three trials using an orally administered, once-daily fixed-dose combination of ledipasvir, an NS5A inhibitor, and Sovaldi (sofosbuvir), an NS5B inhibitor.

In the trials, a total of 1,952 patients were randomized to receive ledipasvir 90 mg/Sovaldi 400 mg, with or without ribavirin,* for a treatment period of eight, 12 or 24 weeks. Of these patients, 1,512 were treatment-naïve, 440 were treatment-experienced and 224 had compensated cirrhosis. The primary endpoint of each trial was the proportion of patients with sustained virologic response 12 weeks after completing therapy (SVR12). Of the 1,518 patients with SVR12 results, 95.9 percent achieved the primary endpoint of attaining an SVR12.

Fewer side effects were reported in the ribavirin-free groups compared to the groups with ribavirin. The most common side effects reported with ledipasvir/Sovaldi alone were fatigue and headache. In those also taking ribavirin, the most common side effects were fatigue, headache, nausea and insomnia. The incidence of anemia was 0.5 percent in the non-ribavirin groups and 9.2 percent in the ribavirin groups.

The FDA has designated the fixed-dose combination of ledipasvir/Sovaldi as a breakthrough therapy. Gilead filed an NDA in February 2014.

Medications recently approved

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Approval date	Comments
Bleeding disorders					
Biogen Idec/Alprolix (coagulation factor IX (recombinant), Fc fusion protein)	For adults and children with hemophilia B for the control and prevention of bleeding episodes, perioperative management, and routine prophylaxis to prevent or reduce the frequency of bleeding episodes	Replaces deficient factor/Factor replacement therapy	IV injection	3/28/14	• First hemophilia B therapy to reduce bleeding episodes with prophylactic infusions starting at least a week apart
Baxter/Feiba NF* (anti-inhibitor coagulant complex)	For routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A or B who have developed inhibitors	Replaces deficient factor/Factor replacement therapy	IV injection or infusion	12/19/13	• Previously approved for the control of spontaneous bleeding episodes or to cover surgical interventions in patients with hemophilia A or B who have developed inhibitors
Novo Nordisk/Tretten (coagulation factor XIII A-subunit, recombinant)	For routine prophylaxis of bleeding in patients with congenital factor XIII A-subunit deficiency	Replaces deficient factor/Factor replacement therapy	IV injection	12/20/13	• Only recombinant treatment for congenital FXIII A-subunit deficiency
Cystic fibrosis					
Vertex Pharmaceuticals/ Kalydeco (ivacaftor)	For the treatment of cystic fibrosis (CF) in patients age 6 years and older who have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene: *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N*, or *S549R*	Increases chloride ion transport across cell membranes/*CFTR* potentiator	Oral	2/21/14	• Previously approved for *G551D* mutations
Inflammatory diseases					
Celgene/Otezla (apremilast)	For the treatment of adult patients with active psoriatic arthritis (PsA)	Modulates the inflammatory response/ Phosphodiesterase 4 inhibitor	Oral	2/21/14	• Previously approved for *G551D* mutations
Novartis/Xolair* (omalizumab)	For the treatment of adults and adolescents with chronic idiopathic urticaria who remain symptomatic despite H1 antihistamine treatment	Inhibits the binding of immunoglobulin E (IgE)/IgE-directed antibody	Subcutaneous (SC) injection	3/21/14	• Previously approved for the treatment of allergic asthma
Lipodystrophy					
AstraZeneca Myalept* (metreleptin)	As an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy	Reduces fat accumulation in organs/Leptin analogue	SC injection	2/24/14	• First therapy approved by the FDA for generalized lipodystrophy
Lysosomal storage diseases					
BioMarin Pharmaceutical/Vimizim* (elosulfase alfa)	For the treatment of mucopolysaccharidosis type IVA (MPS IVA, Morquio A syndrome)	Replaces deficient *N*-acetylgalactosamine-6-sulfatase/Enzyme replacement therapy	IV infusion	2/14/14	• First therapy approved by the FDA for MPS IVA

*These medications have a boxed warning.

Medications recently approved (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Approval date	Comments
Multiple sclerosis					
Teva Pharmaceuticals/ Copaxone (glatiramer acetate)	For the treatment of patients with relapsing forms of multiple sclerosis (MS)	Modulates the immune system/Disease-modifying therapy	SC injection	1/28/14	• New formulation dosed three times weekly
Neurogenic disorders					
Chelsea Therapeutics/ Northera* (droxidopa)	For the treatment of symptomatic neurogenic orthostatic hypotension (NOH) caused by primary autonomic, dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy	Increases norepinephrine levels in the nervous system/ Synthetic catecholamine	Oral	2/18/14	• First therapy approved which demonstrates symptomatic benefit in patients with NOH
Oncology					
GlaxoSmithKline/Mekinist (trametinib)	In combination with Tafinlar (dabrafenib) for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test	Inhibits cell growth and survival/Mitogen-activated extracellular signal regulated kinase (MEK) inhibitor	Oral	1/8/14	• Previously approved as a single agent for melanoma with V600E or V600K mutations
GlaxoSmithKline/Tafinlar (dabrafenib)	In combination with Mekinist (trametinib) for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test	Inhibits cell growth and survival/BRAF kinase inhibitor	Oral	1/9/14	• Previously approved as a single agent for melanoma with V600E mutations
Pharmacyclics/Imbruvica (ibrutinib)	For the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy	Inhibits cell growth and survival/Bruton's tyrosine kinase (BTK) inhibitor	Oral	2/12/14	• Previously approved for the treatment of mantle cell lymphoma (MCL)
Pulmonary hypertension					
United Therapeutics/Orenitram (treprostinil)	For the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity	Dilates pulmonary blood vessels/Prostacyclin analogue	Oral	12/20/13	• First orally administered prostacyclin analogue approved by the FDA

*These medications have a boxed warning.

Pipeline medications in phase III trials

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Bleeding disorders				
Baxter/BAX 855 (recombinant factor VIII)	For the treatment and prevention of bleeding in patients with hemophilia A	Replaces deficient factor/Factor replacement therapy	IV infusion	• Completed enrollment of phase III trial November 2013 • Regulatory filings planned for late 2014
Baxter/OBI-1 (recombinant antihemophilic porcine sequence factor VIII)	For the treatment of bleeding in patients with acquired hemophilia A	Replaces deficient factor/Factor replacement therapy	IV infusion	• Designated as an orphan drug with fast-track status • BLA filed December 2013
Biogen Idec/Eloctate (recombinant factor VIII Fc fusion protein)	For the treatment and prevention of bleeding in patients with hemophilia A	Replaces deficient factor/Factor replacement therapy	IV infusion	• BLA filed March 2013 • FDA requested additional information related to the manufacturing process November 2013 • A response to the BLA is expected June 2014
Cystic fibrosis				
Vertex Pharmaceuticals/ Lumacaftor (VX-809)	In combination with Kalydeco (ivacaftor) in patients with CF who have two copies of the F508del mutation in the *CFTR* gene	Increases the movement of *CFTR* to the cell surface/*CFTR* corrector	Oral	• Designated as an orphan drug • FDA granted breakthrough therapy designation • NDA filing planned for the second half of 2014
Endocrine disorders				
NPS Pharmaceuticals/Natpara (recombinant human parathyroid hormone)	For the treatment of hypoparathyroidism	Replaces deficient hormone/ Hormone replacement therapy	SC injection	• BLA filed October 2013 • A response to the BLA is expected October 2014
Fertility				
Merck/Corifollitropin alfa	For the development of multiple follicles and pregnancy in women participating in an assisted reproductive technology program	Stimulates ovarian follicular growth/ Sustained follicle stimulant	SC injection	• FDA accepted NDA for standard review September 2013
Growth disorders				
Aeterna Zentaris/Macimorelin acetate	For the evaluation adult growth hormone deficiency	Stimulates the secretion of growth hormone/Ghrelin receptor agonist	Oral	• NDA filed November 2013 • A response to the NDA is expected November 2014

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Hepatitis				
AbbVie/ABT-450 + ritonavir* ABT-267 ABT-333	In combination with ribavirin for the treatment of chronic HCV infection in genotype 1 patients	Prevents virus replication/Protease inhibitor (ABT-450 + ritonavir), NS5A inhibitor (ABT-267), non-nucleoside polymerase inhibitor (ABT-333)	Oral	• FDA granted breakthrough therapy designation • Regulatory submissions planned for second quarter 2014
Gilead Sciences/Ledipasvir	In fixed-dose combination with Sovaldi (sofosbuvir) for the treatment of chronic HCV infection in genotype 1 patients	Prevents virus replication/NS5A inhibitor	Oral	• FDA granted breakthrough therapy designation • NDA filed February 2014
Hereditary angioedema				
Pharming Group NV and Salix Pharmaceuticals/Ruconest (C1 inhibitor)	For the treatment of acute attacks in patients with hereditary angioedema	Replaces deficient C1 inhibitor/ C1 inhibitor replacement therapy	IV infusion	• Designated as an orphan drug • BLA filed April 2013 • A response to the BLA is expected April 2014
Human immunodeficiency virus				
Immune Response BioPharma/ Remune	To boost the immune system in HIV patients receiving antiviral treatment	Induces an HIV-specific T-cell response/Therapeutic vaccine	Injection	• Designated as an orphan drug for pediatric patients • BLA filing planned for early 2014
Inflammatory diseases				
Novartis/ Secukinumab (AIN457)	For the treatment of plaque psoriasis	Interferes with the inflammatory response/IL-17A inhibitor	SC injection	• BLA filed October 2013 • A response to the BLA is expected October 2014
Sanofi and Regeneron Pharmaceuticals/Sarilumab	For the treatment of rheumatoid arthritis (RA)	Interferes with the inflammatory response/IL-16 inhibitor	SC injection	• Co-primary endpoints achieved in phase III trial November 2013 • Four other phase III trials ongoing
Takeda/Entyvio (vedolizumab)	For the treatment of moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC)	Modulates the inflammatory response/α4β7 integrin inhibitor	IV infusion	• BLAs filed June 2013 • FDA granted priority review status to UC application and standard review to CD application • A response to the BLA for UC is expected May 2014 and for CD June 2014
Lambert Eaton Myasthenic Syndrome				
Catalyst Pharmaceutical Partners/ Firdapse (amifampridine phosphate)	For the treatment of Lambert-Eaton myasthenic syndrome	Improves impulse conduction in nerve fibers/Potassium channel blocker	Oral	• Designated as an orphan drug • FDA granted breakthrough therapy designation • Phase III results are expected second quarter 2014

*These medications have a boxed warning.

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Lysosomal storage diseases				
Amicus Therapeutics and GlaxoSmithKline/Amigal (migalastat HCl)	For the treatment of Fabry disease	Binds to and stabilizes alpha-galactosidase/Alpha-galactosidase A enhancer	Oral	• Designated as an orphan drug • Primary endpoint not achieved in stage I of first phase III trial December 2012 • Stage II results are expected second quarter 2014
Genzyme/Cerdelga (eliglustat)	For the treatment of adult patients with Gaucher disease type 1	Reduces the production of glucosylceramide/Glucosylceramide synthase inhibitor	Oral	• Designated as an orphan drug • NDA accepted and granted priority review December 2013
Synageva BioPharma/ Sebelipase alfa	For the treatment of early and late onset lysosomal acid lipase (LAL) deficiency	Replaces deficient LAL/Enzyme replacement therapy	IV infusion	• Designated as an orphan drug with fast-track status • FDA granted breakthrough therapy designation for early onset LAL deficiency • Top-line phase III results are expected second half 2014
Multiple sclerosis				
Biogen Idec/Plegridy (peginterferon beta-1a)	For the treatment of relapsing-remitting MS	Unknown mechanism of action in MS/Interferon	SC injection	• Dosed once every two or four weeks • FDA granted fast-track status • BLA filed May 2013 • A response to the BLA was expected March 2014; however, the FDA has extended the review period • A response is now expected June 2014
Teva Pharmaceuticals/Laquinimod	For the treatment of relapsing-remitting MS	Inhibits autoimmune and inflammatory disease activity/ Immunomodulatory agent	Oral	• Third phase III trial is ongoing • This trial is being conducted under a special protocol assessment
Oncology				
Cell Therapeutics/Opaxio (paclitaxel poliglumex)	For the treatment of ovarian cancer	Inhibits cell division/ Microtubule inhibitor	IV infusion	• Links paclitaxel to a biodegradable polyglutamate polymer that delivers more chemotherapy to tumor cells • Completed enrollment of phase III trial January 2014
Eisai/Lenvatinib	For the treatment of radioiodine-refractory differentiated thyroid cancer	Inhibits cell growth and survival/ Tyrosine kinase inhibitor (TKI)	Oral	• Designated as an orphan drug • NDA filing planned for 2014
Eli Lilly/Necitumumab	For the treatment of non-small cell lung cancer (NSCLC)	Reduces tumor cell growth and blood supply/Epidermal growth factor receptor inhibitor	IV infusion	• Primary endpoint achieved in phase III trial • Filing anticipated by the end of 2014

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Oncology				
Eli Lilly/Ramucirumab	For the second-line treatment of gastric cancer and in combination with chemotherapy for the second-line treatment of NSCLC	Reduces tumor cell growth and blood supply/VEGF receptor inhibitor	IV infusion	• Designated as an orphan drug for gastric cancer • BLA for gastric cancer filed fourth quarter 2013 • FDA granted priority review status • A response to the BLA is expected second quarter 2014 • Regulatory filing for NSCLC expected end of 2014
Gilead Sciences/Idelalisib	For the treatment of indolent non-Hodgkin's lymphoma (iNHL) and in combination with Rituxan* (rituximab) for the treatment of relapsed CLL	Inhibits cell growth and survival/ Phosphoinositide 3-kinase inhibitor	Oral	• Designated as an orphan drug for CLL indication • FDA granted breakthrough therapy designation for CLL indication • NDA for iNHL filed September 2013 and for CLL December 2013 • A response to the NDA for iNHL is expected September 2014
Janssen/Siltuximab	For the treatment of MCD in patients who are HIV-negative and human herpes virus 8-negative	Interferes with the inflammatory response/IL-6 inhibitor	IV infusion	• Designated as an orphan drug • BLA filed September 2013 • FDA granted priority review status • A response to the BLA is expected May 2014
Merck/Lambrolizumab (MK-3475)	For the treatment of patients with advanced melanoma who have been previously treated with Yervoy* (ipilimumab)	Antiprogrammed cell death 1 (PD-1) immunotherapy	IV infusion	• FDA granted breakthrough therapy designation • Initiated rolling BLA submission January 2014; expecting to complete the application first half 2014
Novartis and Array BioPharma/ Binimetinib	For the treatment of NRAS mutant melanoma	Inhibits cell growth and survival/ MEK inhibitor	Oral	• Designated as an orphan drug • Regulatory filings planned for 2015
Novartis/Ceritinib (LDK378)	For the treatment of anaplastic lymphoma kinase positive (ALK+) NSCLC in patients previously treated with Xalkori (crizotinib)	Inhibits cell growth and survival/ ALK inhibitor	Oral	• Designated as an orphan drug • FDA granted breakthrough therapy designation • NDA filed fourth quarter 2013
Novartis/Midostaurin	For treatment of patients with FLT-3 mutated acute myeloid leukemia (AML)	Inhibits cell growth and survival/ Signal transduction inhibitor	Oral	• Designated as an orphan drug • Regulatory filings planned for 2015

*These medications have a boxed warning.

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Oncology				
Novartis/Panobinostat	For the treatment of relapsed or refractory multiple myeloma (MM)	Inhibits cell growth and survival/Histone deacetylase inhibitor	Oral	• Designated as an orphan drug • Primary endpoint achieved in phase III trial December 2013 • Regulatory filings planned for 2014
Onconova Therapeutics/Rigosertib	For the treatment of refractory myelodysplastic syndromes (MDS)	Targets alpha and beta isoforms of PI-3 kinase/Multikinase inhibitor	IV infusion	• An oral formulation is also in development • Primary endpoint not achieved in phase III trial February 2014
Pfizer/Palbociclib	In combination with letrozole for the treatment of breast cancer	Prevents tumor cell progression/ Cyclin-dependent kinase inhibitor	Oral	• FDA granted breakthrough therapy designation • Primary endpoint achieved in phase II trial February 2014 • Phase III trials ongoing
Spectrum Pharmaceuticals/ Beleodaq (belinostat)	For the treatment of relapsed or refractory peripheral T-cell lymphoma	Inhibits cell growth and survival/Histone deacetylase inhibitor	IV infusion	• Designated as an orphan drug • NDA filed December 2013 • FDA granted priority review status • A response to the NDA is expected August 2014
Primary immunodeficiency				
Baxter and Halozyme/HyQvia (immune globulin with recombinant human hyaluronidase)	For the treatment of adult patients with primary immunodeficiency	Replaces deficient immunoglobulin/ Replacement therapy	SC infusion	• BLA filed July 2011 • Received complete response letter August 2012 • Amended BLA filed fourth quarter 2013
Pulmonary hypertension				
Actelion/Selexipag	For the treatment of PAH	Reduces vascular smooth muscle constriction/Prostacyclin receptor agonist	Oral	• Designated as an orphan drug • Results from phase III trial expected mid-2014

New dosage forms in the pipeline

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Current route of administration	Investigational route of administration	Comments
Human immunodeficiency virus					
Viiv Healthcare/Trii (dolutegravir, abacavir,* lamivudine*)	For the treatment of HIV	Prevents virus replication/Integrase inhibitor, nucleoside reverse transcriptase inhibitors	Oral	Oral	• Single-tablet regimen • NDA filed October 2013
Multiple sclerosis					
Biogen Idec and AbbVie/ Daclizumab HYP (high-yield process)	For the treatment of relapsing-remitting MS	Binds to the CD25 receptor on T-cells/ Therapeutic antibody	IV infusion	SC injection	• Phase III results expected 2014 • Previously marketed as Zenapax* for the prevention of acute kidney rejection
Neuroendocrine disorders					
Novartis/Signifor LAR (pasireotide long-acting release)	For the treatment of acromegaly	Binds somatostatin receptors/Somatostatin analogue	SC injection	Intramuscular (IM) injection	• Monthly IM injection • Primary endpoint achieved in phase III trial July 2013 • Regulatory submissions planned for 2014

*These medications have a boxed warning.
†Dosage form is not available. Only investigational route of administration is available at this time.

New indications in pipeline

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/ Drug class	Route of administration	Comments
Inflammatory diseases					
AbbVie/Humira* (adalimumab)	For the treatment of RA, polyarticular juvenile idiopathic arthritis, PsA, ankylosing spondylitis, CD, UC and psoriasis	For the treatment of hidradenitis suppurativa	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	• Results from phase III trials are expected 2014
Celgene/Otezla (apremilast)	For the treatment of adult patients with active PsA	For the treatment of psoriasis	Modulates the inflammatory response/ Phosphodiesterase 4 inhibitor	Oral	• NDA filed September 2013 • A response to the NDA is expected September 2014
Multiple sclerosis					
Genzyme/Lemtrada (alemtuzumab)	For the treatment of B-cell CLL	For the treatment of relapsing MS	Binds to the CD52 antigen on B-cells and T-cells/Therapeutic antibody	IV injection	• FDA granted fast track status • sBLA filed June 2012 • Received a complete response letter December 2013; the FDA recommended an additional clinical trial • Marketed as Campath* for CLL indication
Oncology					
Celgene/Revlimid* (lenalidomide)	For the treatment of previously treated MM, MDS and relapsed or refractory MCL	For the treatment of newly diagnosed MM	Possesses immuno-modulatory, anti-inflammatory and antiangiogenic properties/ Thalidomide analogue	Oral	• Primary endpoint achieved in phase III trial July 2013 • sNDA filing planned for first quarter 2014
GlaxoSmithKline/ Votrient* (pazopanib)	For the treatment of renal cell carcinoma and soft tissue sarcoma	For the treatment of advanced epithelial ovarian cancer	Inhibits cell growth and survival/TKI	Oral	• Designated as an orphan drug • Primary endpoint achieved in phase III trial June 2013
GlaxoSmithKline and Genmab/Arzerra* (ofatumumab)	For the treatment of patients with CLL refractory to fludarabine* and alemtuzumab*	In combination with an alkylator-based therapy for the treatment of CLL in patients who are treatment-naïve or ineligible for fludarabine-based therapy	Targets the CD20 protein on malignant B-cells/Anti-CD20 antibody	IV infusion	• FDA granted breakthrough therapy designation • sBLA filed October 2013 • FDA granted priority review status • A response to the sBLA is expected April 2014
Incyte Corporation/ Jakafi (ruxolitinib)	For the treatment of patients with intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF	For the treatment of polycythemia vera	Inhibits the formation and development of blood cells/Janus kinase (JAK) inhibitor	Oral	• Designated as an orphan drug with fast-track status • Primary enpoint achieved in phase III trial March 2014 • sNDA filing planned for first half 2014

*These medications have a boxed warning.

New indications in pipeline (continued)

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/ Drug class	Route of administration	Comments
Oncology					
Medivation and Astellas Pharma/Xtandi (enzalutamide)	For the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) who have previously received docetaxel	For the treatment of patients with chemotherapy-naïve mCRPC	Inhibits cell growth and survival/ Androgen receptor inhibitor	Oral	• sNDA filed March 2014
Ophthalmology					
Regeneron Pharmaceuticals/ Eylea (aflibercept)	For the treatment of neovascular (wet) age-related macular degeneration and macular edema following central retinal vein occlusion	For the treatment of diabetic macular edema (DME) and macular edema following branch retinal vein occlusion (BRVO)	Binds vascular endothelial growth factor and placental growth factor/ Antiangiogenesis inhibitor	Intravitreal injection	• sBLA for DME accepted December 2013 and sBLA for macular edema following BRVO accepted February 2014 • A response to the sBLA for DME is expected August 2014 and for macular edema following BRVO October 2014

Glossary of terms

Antibody-drug conjugate
Consists of a monoclonal antibody linked to a cytotoxic drug.

BLA
Stands for "biologics license application," similar to an NDA but used for investigational medications that are considered to be biologic agents.

Breakthrough therapy designation
Intended to expedite the development and review of a potential new drug for serious or life-threatening diseases.

Complete response letter
Issued to let the applicant know that the review period for an investigational agent is complete, and that the NDA or BLA is not yet ready for approval.

Double-blind trial
A type of study in which the participants and the investigators are blinded to treatment. This type of study has less bias than nonblinded studies.

Fast track
Designation granted by the FDA to an investigational agent indicating an expedited review of the NDA or BLA; usually applies to medications that treat serious or life-threatening conditions and demonstrate the potential to address unmet medical needs.

NDA
Stands for "new drug application," the process by which a manufacturer submits information to the FDA to gain approval for the agent; conducted after phase III development is completed.

Orphan drug
A medication that treats a rare disease that affects fewer than 200,000 Americans. A medication granted orphan drug status is entitled to seven years of marketing exclusivity.

Phase III
Last phase of medication development; involves safety and efficacy trials of the new medication. This phase of development can take years to complete.

Priority review
Designation granted by the FDA to an investigational agent after it has been submitted to the FDA for approval. A priority designation means that the FDA will review and take action on the application (approve or not approve) within six months instead of the standard 10 months for all other medication filings.

Refusal to file letter
A letter the FDA issues to the applicant if it determines the application is not sufficiently complete.

Rolling submission
Usually applies to fast-track medications; indicates that the review process can be started even before the FDA receives all the information. However, the FDA requires all the information before a final decision about approval can be made.

sBLA
Stands for "supplemental biologics license application," similar to sNDA but used for already approved investigational medications that are considered to be biologic agents.

sNDA
Stands for "supplemental new drug application," the process by which a pharmaceutical company submits information to the FDA to gain approval for a new indication for an agent that has already been approved by the FDA.

SPA
Stands for "special protocol assessment," an agreement with the FDA that the manufacturer's clinical protocol for a phase III trial is acceptable to support an NDA or BLA.

Treatment-naive
Patients who have never been treated before for a particular condition.

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Manufacturers' websites

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Information in the report is current as of March 2014, and was accessed on March 28, 2014.

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