Pipeline Report

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

First quarter 2014

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.

This report is not intended to be used 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.

Ramucirumab

Eli Lilly has filed a biologics license application (BLA) for ramucirumab as a single-agent treatment for advanced gastric cancer following disease progression after initial chemotherapy. Ramucirumab is a vascular endothelial growth factor (VEGF) receptor inhibitor that reduces tumor cell growth and blood supply.

The BLA filing was based on a randomized, double-blind, phase III trial. Patients who had failed a first-line chemotherapy treatment were enrolled and assigned to receive ramucirumab (238 patients) or placebo (117 patients). Ramucirumab was administered as an intravenous (IV) infusion at a dose of 8 mg/kg every two weeks. Patients in both groups also received best supportive care, as determined by their physician. The primary endpoint of the trial was overall survival (OS). Median OS in the ramucirumab group was 5.2 months, compared to 3.8 months in the placebo group. This difference was considered statistically significant. Hypertension was reported more frequently in the ramucirumab group than the placebo group.

Ramucirumab is designated as an orphan drug. The FDA accepted the BLA filing and granted priority review status to the application. A response to the BLA is expected in the second quarter of 2014.

Vedolizumab

Takeda has developed vedolizumab for the treatment of moderately to severely active Crohn's disease (CD) or ulcerative colitis (UC). Vedolizumab is a monoclonal antibody directed against α4β7 integrin, which is found on certain white blood cells that have been shown to play a role in the inflammatory response.

The phase III program consisted of four trials to evaluate the efficacy of vedolizumab on clinical response and remission (along with effect on mucosal healing in UC), and long-term safety in patients with CD and UC who had failed at least one conventional therapy or a tumor necrosis factor (TNF) alpha inhibitor. Three of the trials were placebo-controlled, while one was an open-label trial. In all of the trials, 300 mg of vedolizumab was administered as an IV infusion at weeks zero, two and six and then every four or eight weeks thereafter.

Two separate BLAs were filed, one for CD and one for UC, in June 2013. The FDA granted priority review status to the application for UC and standard review to the application for CD.

ABT-450, ABT-267, ABT-333

AbbVie has developed three investigational direct-acting antiviral agents to be used for the treatment of chronic hepatitis C virus (HCV). This all-oral 3D regimen includes a boosted protease inhibitor (ABT-450 plus ritonavir*), an NS5A inhibitor (ABT-267) and a non-nucleoside polymerase inhibitor (ABT-333) in combination with ribavirin.*

The phase III program for this treatment regimen includes six trials in patients with genotype 1 HCV. The results of the first trial, SAPPHIRE-I, were recently reported. In this randomized, double-blind, placebo-controlled trial, 631 treatment-naïve genotype 1 HCV patients with no liver cirrhosis were enrolled and assigned to the 3D regimen plus ribavirin for 12 weeks (473 patients) or placebo for the first 12 weeks (158 patients). Patients who were initially assigned to the placebo group then received open-label treatment with the 3D regimen plus ribavirin for 12 weeks. The regimen is administered as a fixed-dose combination of ABT-450/ritonavir (150 mg/100 mg) coformulated with ABT-267 (25 mg) dose once daily in combination with ABT-333 (250 mg) and ribavirin (weight-based), both dosed twice daily.

The primary endpoint of SAPPHIRE-I was the percentage of subjects with sustained virologic response 12 weeks (SVR12) post treatment. After 12 weeks of active treatment, 96 percent (455 of 473) of patients achieved an SVR12. The most common adverse events reported were fatigue, headache and nausea. AbbVie expects the results from the other five trials in the coming months, and is planning regulatory submissions for approval of the 3D regimen in the second quarter of 2014. The FDA has designated the 3D regimen as a breakthrough therapy.

Medications recently approved

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Approval date	Comments
Bleeding disorders					
Novo Nordisk/ Novoeight (turoctocog alfa)	For use in adults and children with hemophilia A for control and prevention of bleeding episodes, for perioperative management and for routine prophylaxis to prevent or reduce the frequency of bleeding episodes	Replaces deficient factor/Factor replacement therapy	IV infusion	10/15/13	• Launch planned for shortly after April 2015
Hepatitis					
Gilead Sciences/ Sovaldi (sofosbuvir)	For the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen	Prevents virus replication/ Nucleotide analog NS5B polymerase inhibitor	Oral	12/6/13	• First all-oral treatment regimen approved for gneotypes 2 and 3
Janssen and Medivir AB/ Olysio (simeprevir)	For the treatment of CHC infection as a component of a combination antiviral treatment regimen	Prevents virus replication/NS3/4A protease inhibitor	Oral	11/22/13	• First once-daily protease inhibitor approved for the treatment of CHC
Inflammatory diseases					
Genentech/ Actemra* (tocilizumab)	For the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs)	Blocks Interleukin (IL)-6 receptors/ Monoclonal antibody	Subcutaneous (SC) injection	10/21/13	• Previously approved as an IV infusion for the treatment of RA, polyarticular juvenile idiopathic arthritis (PJIA) and systemic juvenile idiopathic arthritis (SJIA)
Janssen/Stelara (ustekinumab)	For the treatment of adult patients with active psoriatic arthritis (PsA)	Targets IL-12 and IL-23/Dual IL inhibitor	SC injection	9/20/13	• Previously approved for the treatment of psoriasis
UCB Pharma/ Cimzia* (certolizumab pegol)	For the treatment of adult patients with active PsA and for the treatment of adults with active ankylosing spondylitis (AS)	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	PsA 9/27/13 AS 10/17/13	• Previously approved for the treatment of CD and RA

Pipeline medications in phase III trials

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Approval date	Comments
Oncology					
Bayer HealthCare and Onyx Pharmaceuticals/ Nexavar (sorafenib)	For the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma that is refractory to radioactive iodine treatment	Inhibits cell growth and survival/ Tyrosine kinase inhibitor (TKI)	Oral	11/22/13	• Previously approved for the treatment of hepatocellular carcinoma (HCC) and renal cell carcinoma (RCC)
Genentech/ Gazyva* (obinutuzumab)	In combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)	Targets the CD20 protein on malignant B-cells/ Anti-CD20 antibody	IV infusion	11/1/13	• First product approved with the FDA's breakthrough therapy designation
Pharmacyclics/ Imbruvica (ibrutinib)	For the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy	Inhibits cell growth and survival/ Bruton's tyrosine kinase (BTK) inhibitor	Oral	11/13/13	• First BTK inhibitor approved
Roche/Perjeta* (pertuzumab)	In combination with Herceptin* (trastuzumab) and docetaxel* for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory or early stage breast cancer	Prevents the HER2 receptor from pairing with other HER receptors/ HER2 receptor antagonist	IV infusion	9/30/13	• Previously approved for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease
Pulmonary hypertension					
Actelion/ Opsumit* (macitentan)	For the treatment of pulmonary arterial hypertension (PAH, WHO Group 1)	Reduces vascular smooth muscle constriction/ Endothelin receptor antagonist	Oral	10/18/13	• Walgreens Specialty Pharmacy is a distributor of this medication
Bayer HealthCare/ Adempas* (riociguat)	For the treatment of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH, WHO Group 4) after surgical treatment or inoperable CTEPH and for the treatment of PAH, WHO Group 1	Reduces vascular smooth muscle constriction/Soluble guanylate cyclase stimulator	Oral	10/8/13	• First product approved for CTEPH indication
Peyronie's disease					
Auxilium Pharmaceuticals/ Xiaflex* (collagenase clostridium histolyticum)	For the treatment of adult men with Peyronie's disease (PD) with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy	Breaks down collagen deposits/ Purified collagenase	Injection	12/6/13	• First product approved as an effective treatment for PD

Pipeline medications in phase III trials

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Bleeding disorders				
Baxter/BAX 855	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
Biogen Idec/Alprolix (recombinant factor IX Fc fusion protein)	For the treatment and prevention of bleeding in patients with hemophilia B	Replaces deficient factor/Factor replacement therapy	IV infusion	• BLA filed January 2013 • A response to the BLA was expected January 2014; however, the FDA has extended the review period • A response is now expected April 2014
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 in November 2013
Cystic fibrosis				
Vertex Pharmaceuticals/ Lumacaftor (VX-809)	In combination with Kalydeco (ivacaftor) in patients with cystic fibrosis (CF) who have two copies of the F508del mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene	Increases the movement of *CFTR* to the cell surface/*CFTR* corrector	Oral	• FDA granted breakthrough therapy designation • Data from two phase III trials expected in 2014, followed by new drug application (NDA) submission
Duchenne muscular dystrophy				
Sarepta Therapeutics/ Eteplirsen	For the treatment of Duchenne muscular dystrophy (DMD)	Restores protein translation and dystrophin production/RNA modulator	IV infusion	• Designated as an orphan drug with fast-track status • NDA filing was planned for the first half of 2014; however, the FDA has indicated that a confirmatory trial should be conducted before filing for approval
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
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

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 • Results of first phase III trial reported November 2013 • Regulatory submissions planned for the second quarter of 2014
Gilead Sciences/ Ledipasvir	In fixed-dose combination with sofosbuvir with or without ribavirin for the treatment of chronic HCV infection in genotype 1 patients	Prevents virus replication/NS5A inhibitor	Oral	• Three phase III trials ongoing • Regulatory submissions planned for the second quarter of 2014
Hereditary angioedema				
Pharming Group NV and Santarus/ 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				
Gilead Sciences/ Cobicistat	To increase blood levels of certain protease inhibitors to enable once-daily dosing	Inhibits cytochrome P4503A/ Pharmacoenhancer	Oral	• NDA filed June 2012 • Received a complete response letter April 2013 • Gilead is addressing the FDA's concerns with the NDA
Gilead Sciences/ Elvitegravir	For the treatment of HIV in treatment-experienced patients	Prevents virus replication/Integrase inhibitor	Oral	• NDA filed June 2012 • Received a complete response letter April 2013 • Gilead is addressing the FDA's concerns with the NDA

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Inflammatory diseases				
Celgene/ Apremilast	For the treatment of PsA and psoriasis	Modulates the inflammatory response/ Phosphodiesterase type 4 inhibitor	Oral	• NDA filed for PsA March 2013 • NDA filing for psoriasis is expected in the fourth quarter of 2013
Novartis/ Secukinumab (AIN457)	For the treatment of plaque psoriasis	Interferes with the inflammatory response/ IL-17A inhibitor	SC injection	• Primary endpoint achieved in phase III trial July 2013 • Regulatory filings expected in the fourth quarter of 2013
Sanofi and Regeneron Pharmaceuticals/ Sarilumab	For the treatment of 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/ Vedolizumab	For the treatment of moderately to severely active CD and 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
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 expected in the second quarter of 2014
Lipodystrophy				
Bristol-Myers Squibb and AstraZeneca/ Metreleptin	For the treatment of metabolic disorders associated with inherited or acquired lipodystrophy	Reduces fat accumulation in organs/Leptin analogue	SC injection	• Designated as an orphan drug • BLA accepted and granted priority review June 2013 • A response to the BLA is expected February 2014

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 in the fourth quarter of 2013
BioMarin Pharmaceutical/ Vimizim (GALNS)	For the treatment of MPS IVA (Morquio A syndrome)	Replaces deficient N-acetylgalactosamine-6-sulfatase (GALNS)/Enzyme replacement therapy	IV infusion	• Designated as an orphan drug • BLA filed April 2013 • FDA granted priority review status • A response to the BLA is expected February 2014
Genzyme/ Cerdelga (eliglustat)	For the treatment of Gaucher's disease	Reduces the production of glucocerebroside/ Glucosylceramide synthase inhibitor	Oral	• Designated as an orphan drug • NDA accepted and granted priority review June 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	• FDA granted breakthrough therapy designation for early onset LAL deficiency • Designated as an orphan drug with fast-track status • Enrollment in the phase III trial for late onset LAL deficiency completed December 2014
Multiple sclerosis				
Biogen Idec/ Plegridy (peginterferon beta-1a)	For the treatment of relapsing-remitting multiple sclerosis (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
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
Neurogenic disorders				
Chelsea Therapeutics/ Northera (droxidopa)	For the treatment of symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, dopamine beta-hydroxylase deficiency and nondiabetic autonomic neuropathy	Increases norepinephrine levels in the nervous system/Synthetic catecholamine	Oral	• Designated as an orphan drug with fast-track status • Received a complete response letter March 2012 • FDA accepted resubmission of NDA • A response to the NDA is expected February 2014

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Neutropenia				
Teva Pharmaceuticals/ Balugrastim	To reduce the duration of severe neutropenia in cancer patients undergoing chemotherapy	Long-acting granulocyte colony-stimulating factor	SC injection	• BLA filed December 2012 • BLA withdrawn after discussions with the FDA November 2013
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 • Phase III trial ongoing
Eisai/Lenvatinib	For the treatment of thyroid cancer	Inhibits cell growth and survival/TKI	Oral	• Designated as an orphan drug
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
Eli Lilly/ Ramucirumab	For the second-line treatment of gastric cancer	Reduces tumor cell growth and blood supply/VEGF receptor inhibitor	IV infusion	• Designated as an orphan drug • BLA filed in the fourth quarter of 2013 • FDA granted priority review status • A response to the BLA is expected in the second quarter 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	• FDA granted breakthrough therapy designation for CLL indication • NDA for iNHL filed September 2013
Janssen/ Siltuximab	For the treatment of multicentric Castleman disease 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
Novartis/ 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	• FDA granted breakthrough therapy designation • NDA filing planned for 2014
Novartis/ Panobinostat	For the treatment of relapsed or refractory multiple myeloma (MM)	Inhibits cell growth and survival/Histone deacetylase inhibitor	Oral	• Primary endpoint achieved in phase III trial December 2013 • Regulatory filings planned for 2014

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Oncology				
Onconova Therapeutics/ Rigosertib	For the treatment of refractory myelodysplastic syndromes (MDS)	Targets alpha and beta isoforms of PI-3 kinases/Multikinase inhibitor	IV infusion	• An oral formulation is also in development • Phase III data expected at the end of 2013 or early 2014
Pfizer/ Palbociclib	For the treatment of breast cancer	Prevents tumor cell progression/ Cyclin-dependent kinase inhibitor	Oral	• FDA granted breakthrough therapy designation • Phase III trials ongoing
Sanofi/ Fedratinib (SAR302503)	For the treatment of myelofibrosis (MF)	Inhibits the formation and development of blood cells/Janus-associated kinase inhibitor	Oral	• Primary endpoint achieved in phase III trial May 2013 • Sanofi cancelled development plans after determining that the safety risks of fedratinib outweigh the potential benefits to patients
Spectrum Pharmaceuticals/ 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
Pulmonary hypertension				
Actelion/ Selexipag	For the treatment of PAH	Reduces vascular smooth muscle constriction/ Prostacyclin receptor agonist	Oral	• Results from phase III trial expected in 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
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 in 2014 • Previously marketed as Zenapax* for the prevention of acute kidney rejection
Teva Pharmaceuticals/ Copaxone (glatiramer acetate)	For the treatment of relapsing-remitting MS	Modulates the immune system/ Disease-modifying therapy	SC injection	SC injection	• Higher dose formulation administered three times a week instead of daily • Supplemental new drug application (sNDA) accepted May 2013
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
Oncology					
Roche/Herceptin (trastuzumab)	For the treatment of HER2-positive early breast cancer	Inhibits the proliferation of tumor cells that overexpress HER2/Monoclonal antibody	IV infusion	SC injection	• Coprimary endpoints achieved in phase III trial October 2011 • Additional studies are currently ongoing
Pulmonary hypertension					
United Therapeutics/ Treprostinil diolamine	For the treatment of PAH	Dilates pulmonary blood vessels/ Prostacyclin analogue	Continuous SC or IV infusion and inhalation	Oral	• Received first complete response letter October 2012 • Received second complete response letter March 2013 • FDA accepted resubmission of NDA • A response to the NDA is expected February 2014

†Dosage form is not available. Only investigational route of administration is available at this time.

New indications in the pipeline

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/Drug class	Route of administration	Comments
Bleeding disorders					
Baxter/Feiba NF* (anti-inhibitor coagulant complex)	For the treatment of bleeding episodes or to cover surgical interventions in patients with hemophilia A or B with inhibitors	For the prevention of bleeding in patients with hemophilia A or B and inhibitors	Replaces deficient factor/ Factor replacement therapy	IV infusion	• Supplemental biologics license application (sBLA) filed February 2013
Cystic fibrosis					
Vertex Pharmaceuticals/ Kalydeco (ivacaftor)	For the treatment of CF in patients ages 6 and older who have a *G551D* mutation in the *CFTR* gene	For the treatment of CF in patients ages 6 and older who have at least one non-*G551D* *CFTR* gating mutation	Increases chloride ion transport across cell membranes/ *CFTR* potentiator	Oral	• Designated as an orphan drug • sNDA filed September 2013
Inflammatory diseases					
AbbVie/Humira* (adalimumab)	For the treatment of RA, PJIA, PsA, AS, 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 in 2014
Novartis/Xolair* (omalizumab)	For the treatment of allergic asthma	For the treatment of chronic idiopathic urticaria	Inhibits the binding of immunoglobulin E (IgE)/IgE-directed antibody	SC injection	• sBLA filing accepted October 2013 • A response to the sBLA is expected in the second quarter of 2014
UCB Pharma/ Cimzia* (certolizumab pegol)	For the treatment of CD, RA, PsA and AS	For the treatment of axial spondyloarthritis	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	• Received a complete response letter October 2013
Multiple sclerosis					
Biogen Idec and Elan/Tysabri* (natalizumab)	For the treatment of relapsing forms of MS (generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy) and for the treatment of CD	For the first-line treatment of relapsing forms of MS in patients who have tested negative for antibodies to the JC virus	Binds and inhibits alpha-4 integrins from adhering to their counter-receptors/ Selective adhesion molecule inhibitors	IV infusion	• sBLA filed January 2013

New indications in the pipeline (continued)

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/Drug class	Route of administration	Comments
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 infusion	• FDA granted fast track status • sBLA filed June 2012 • A response to the sBLA is expected December 2013 • Marketed as Campath* for CLL indication
Oncology					
Celgene/ Revlimid* (lenalidomide)	For the treatment of previously treated MM, MDS and relapsed of 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 the first quarter of 2014
GlaxoSmithKline/ Mekinist (trametinib)	For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations	In combination with Tafinlar for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation	Inhibits cell growth and survival/ Mitogen-activated extracellular signal regulated kinase inhibitor	Oral	• sNDA filed July 2013 • FDA granted priority review • A response to the sNDA is expected January 2014
GlaxoSmithKline/ Tafinlar (dabrafenib)	For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation	In combination with Mekinist for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation	Inhibits cell growth and survival/BRAF kinase inhibitor	Oral	• sNDA filed July 2013 • FDA granted priority review • A response to the sNDA is expected January 2014
GlaxoSmithKline/ Votrient* (pazopanib)	For the treatment of RCC 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

New indications in the pipeline (continued)

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/Drug class	Route of administration	Comments
Oncology					
Incyte Corporation/ Jakafi (ruxolitinib)	For the treatment of patients with intermediate or high-risk 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	• FDA granted fast-track status • Phase III results expected in early 2014 • sNDA filing planned for the first half of 2014
Pharmacyclics/ Imbruvica (ibrutinib)	For the treatment of patients with MCL who have received at least one prior therapy	For the treatment of CLL/small lymphocytic lymphoma (SLL) and Waldenstrom's macro-globulinemia	Inhibits cell growth and survival/BTK inhibitor	Oral	• Designated as an orphan drug • FDA granted breakthrough therapy designation • NDA filed for CLL/SLL July 2013 • FDA granted priority review status
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	Binds vascular endothelial growth factor and placental growth factor/ Anti-angiogenesis inhibitor	Intravitreal injection	• Primary endpoint achieved in two phase III trials August 2013 • sBLA filed in the fourth quarter of 2013

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.

Boxed warning—designated for prescriptions that pose a significant risk of serious or life-threatening adverse effects based on medical studies.

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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