Walgreens

Pipeline Report

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

Third quarter 2012

To help keep you informed about medications in development, the Walgreens pipeline report provides a summary of 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.

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.

Kynamro™ (mipomersen) and lomitapide

Familial hypercholesterolemia (FH) is a genetic disorder characterized by elevated low-density lipoprotein cholesterol (LDL-C) and apolipoprotein B (apoB) levels, resulting in an increased risk of atherosclerosis. Heterozygous FH (HeFH) has a prevalence of approximately one in 500 while homozygous FH (HoFH) has a prevalence of approximately one in one million. In HoFH, LDL-C levels exceed 800 mg/dL beginning in infancy, leading to premature coronary heart disease. Current guidelines for the treatment of FH recommend at least a 50 percent reduction in LDL-C levels, with statins as the preferred initial treatment in both adults and children. While patients with HeFH usually respond very well to statin treatment, the response rate in HoFH is usually less predictable. Many patients with HoFH require artificial clearance of LDL through LDL apheresis, which can reduce LDL-C by approximately 60 percent.

Two products are currently under FDA review for the treatment of HoFH: Kynamro (mipomersen) and lomitapide. Kynamro is an apoB synthesis inhibitor that interferes with the production of LDL-C. In a double-blind, placebo-controlled, phase III trial, 51 patients with HoFH already receiving lipid-lowering therapy were randomized to Kynamro, 200 mg subcutaneous (SC) injection once weekly, or placebo. The primary endpoint of the trial was change in LDL-C from baseline. After 26 weeks, the mean percentage change in LDL-C was significantly greater with Kynamro, 24.7 percent reduction, than with placebo, 3.3 percent reduction. The most common adverse event reported in the trial was injection-site reactions.

Lomitapide is an orally administered microsomal triglyceride transfer protein inhibitor (MTP-I) that interferes with the production of lipoproteins. A single-arm, open-label, phase III trial enrolled 29 patients with HoFH already receiving lipid-lowering therapy. Patients received increasing doses of lomitapide escalated over 26 weeks to a maximum tolerated dose of 60 mg daily. Patients remained on their highest tolerated dose of lomitapide for an additional 52 weeks for safety follow-up. The primary endpoint of the trial was percent change in LDL-C compared to baseline after 26 weeks. The mean percent change in LDL-C was 40.1 percent and the median dose was 40 mg daily. The most common adverse events reported in this trial were gastrointestinal symptoms.

Genzyme and Isis Pharmaceuticals submitted a new drug application (NDA) for Kynamro in March 2012. Aegerion Pharmaceuticals also submitted an NDA for lomitapide in March 2012. Responses to both NDAs are expected in January 2013.

Regorafenib

In April 2012, Bayer HealthCare submitted an NDA for regorafenib for the treatment of metastatic colorectal cancer (mCRC). Regorafenib is an orally administered multikinase inhibitor of vascular endothelial growth factor (VEGF) receptor 2 and tyrosine kinase as well as other kinases.

The efficacy of regorafenib was examined in a double-blind, placebo-controlled, phase III trial of patients with mCRC who had progressed after approved standard therapies. In the trial, 760 patients were randomized to receive best supportive care plus either regorafenib, 160 mg daily for three weeks followed by one week rest, or placebo. The primary endpoint of the trial was overall survival (OS). At the preplanned interim analysis, the primary endpoint was met with median OS rates of 6.4 months in the regorafenib group and 5 months in the placebo group. The most common adverse events reported in this trial were hand-foot syndrome, fatigue, hypertension, diarrhea and rash.

Tivozanib

AVEO Pharmaceuticals and Astellas have developed tivozanib for the treatment of advanced renal cell carcinoma (RCC). Tivozanib is a VEGF receptor inhibitor that inhibits all three VEGF receptors. In an open-label, active comparator-controlled, phase III trial, 517 patients with advanced RCC who were treatment naive or had received no more than one prior systemic therapy were enrolled. Patients were excluded if they had received previous VEGF- or mammalian target of rapamycin (mTOR)-targeted therapy. Patients were randomized to tivozanib, 1.5 mg by mouth once daily for three weeks followed by one week rest, or Nexavar® (sorafenib), 400 mg by mouth twice daily for four weeks with no rest. The primary endpoint of the trial was progression-free survival (PFS). The primary endpoint was met with median PFS of 11.9 months for tivozanib and 9.1 months for Nexavar. Hypertension occurred in 46 percent of patients in the tivozanib group and 36 percent of patients in the Nexavar group. Hand-foot syndrome occurred in 13 percent of patients in the tivozanib group and 54 percent of patients in the Nexavar group. Other common adverse events in both groups were diarrhea, fatigue and neutropenia. Based on the results of this trial, the companies expect to file an NDA for tivozanib in the third quarter of 2012.

Medications recently approved

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Approval date	Comments
Anemia					
Affymax and Takeda/ Omontys® (peginesatide)	For the treatment of anemia due to chronic kidney disease in adult patients on dialysis	Binds to and activates the erythropoietin receptor/ Erythropoiesis stimulating agent	SC or intravenous (IV) injection	3/27/2012	• Administered once a month
Lysosomal storage diseases					
Pfizer and Protalix BioTherapeutics/ Elelyso™ (taliglucerase alfa)	For long-term enzyme replacement therapy (ERT) for adults with Type 1 Gaucher disease	Replaces deficient glucocerebrosidase/ ERT	IV infusion	5/1/2012	• First plant cell-based ERT for Gaucher disease
Oncology					
Genentech/ Perjeta™ (pertuzumab)	In combination with Herceptin® (trastuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease	Prevents the HER2 receptor from pairing with other HER receptors/ HER2 receptor antagonist	IV infusion	6/8/2012	• Targets a different region on the HER2 receptor than Herceptin
GlaxoSmithKline/ Votrient® (pazopanib)	For the treatment of patients with advanced soft tissue sarcoma who have received prior chemotherapy	Inhibits cell growth and survival/ Tyrosine kinase inhibitor (TKI)	Oral	4/26/2012	• Previously approved for the treatment of RCC
Novartis/ Afinitor® (everolimus)	For the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery	Inhibits tumor cell growth and the formation of new mTOR inhibitor	Oral	4/26/2012	• Previously approved for multiple indications

Pipeline medications in phase III trials

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Alzheimer's disease				
Johnson & Johnson and Pfizer/ Bapineuzumab	For the treatment of Alzheimer's disease	Binds to and clears beta amyloid peptide/ Monoclonal antibody immunotherapeutic	IV infusion	• Phase III results expected in the second half of 2012 • Biologics license application (BLA) filing anticipated in 2012-2013
Amyloidosis				
Pfizer/Tafamidis	For the treatment of transthyretin (TTR) familial amyloid polyneuropathy	Inhibits TTR amyloid fibril formation/TTR stabilizer	Oral	• Designated as an orphan drug with fast-track status • Refiled NDA accepted February 2012 • Received a complete response letter June 2012; additional studies are required for approval
Bleeding disorders				
Inspiration Biopharmaceuticals/ IXinity™ (trenonacog alfa, B1001)	For the treatment and prevention of bleeding in patients with hemophilia B	Replaces deficient factor/ Factor replacement therapy	IV infusion	• BLA filed April 2012
Coagulation disorders				
Sanofi-aventis/ Visamerin® (semuloparin)	For the prevention of venous thromboembolism events in cancer patients initiating chemotherapy	Inhibits factor Xa/Ultra-low molecular weight heparin	SC injection	• NDA filed September 2011 • A response to the NDA is expected July 2012
Familial lipid disorders				
Aegerion Pharmaceuticals/ Lomitapide	For the treatment of HoFH	Interferes with the production of lipoproteins/ MTP-I	Oral	• Designated as an orphan drug • NDA filed March 2012 • A response to the NDA is expected January 2013
Genzyme and Isis Pharmaceuticals/ Kynamro™ (mipomersen)	For the treatment of HoFH	Prevents the production of apoB/ApoB synthesis inhibitor	SC injection	• Designated as an orphan drug • NDA filed March 2012 • A response to the NDA is expected January 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	• NDA filing anticipated in 2013

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Hepatitis				
Tibotec Pharmaceuticals/ TMC435	In combination with peginterferon alfa and ribavirin for the treatment of chronic hepatitis C virus (HCV) infection in treatment-naive and treatment-failure patients	Prevents virus replication/Protease inhibitor	Oral	• FDA granted fast-track status • Completed enrollment of three phase III trials August 2011 • NDA filing anticipated in the first half of 2013
Hereditary angioedema				
Pharming Group NV and Santarus/ Rhucin® (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 • Phase III trial expected to be completed by the third quarter of 2012
Human immunodeficiency virus				
Gilead Sciences/ Quad (elvitegravir, cobicistat, emtricitabine and tenofovir)	For the treatment of human immunodeficiency virus (HIV) infection	Prevents virus replication/Integrase inhibitor, boosting agent, nucleoside reverse transcriptase inhibitor and nucleotide reverse transcriptase inhibitor	Oral	• Once-daily, single-tablet regimen • NDA filed October 2011 • A response to the NDA is expected August 2012
Gilead Sciences/ Elvitegravir	For the treatment of HIV in treatment-experienced patients	Prevents virus replication/Integrase inhibitor	Oral	• Primary endpoint achieved in phase III trial March 2011 • NDA filing planned for 2012
Huntington's disease				
NeuroSearch/ Huntexil® (pridopidine)	For the treatment of Huntington's disease	Enhances or inhibits dopamine-dependent functions in the brain/ Dopaminergic stabilizer	Oral	• Designated as an orphan drug • New phase III trial will not be initiated until financing is secured
Inflammatory diseases				
AstraZeneca/ Fostamatinib	For the treatment of rheumatoid arthritis (RA)	Blocks signaling in multiple cell types involved in inflammation and tissue degradation/ Spleen tyrosine kinase (Syk) inhibitor	Oral	• First set of data from phase III trials expected in the second half of 2012 • NDA filing planned for 2013
Pfizer/ Tofacitinib	For the treatment of RA and psoriasis	Interferes with the inflammatory and immune responses/ Janus kinase (JAK) inhibitor	Oral	• NDA filing for RA accepted December 2011 • A response to the NDA is expected August 2012
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 • Second phase III trial initiated in the third quarter of 2011 • Results from the first phase III trial expected in the third quarter of 2012

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Lysosomal storage diseases				
Shire/Replagal® (agalsidase alfa)	For the treatment of Fabry disease	Replaces deficient alpha-galactosidase A/ ERT	IV infusion	• Designated as an orphan drug with fast-track status • Rolling BLA completed November 2011 • FDA granted priority review status • BLA withdrawn March 2012 since additional studies would be required for approval
Multiple sclerosis				
Biogen Idec/ BG-12 (dimethyl fumarate)	For the treatment of relapsing-remitting multiple sclerosis (MS)	Activates the Nrf2 transcriptional pathway, which regulates the antioxidant response/ Gene transcription modulator	Oral	• NDA filed February 2012 • A response to the NDA is expected December 2012
Sanofi-aventis/ Aubagio™ (teriflunomide)	For the treatment of relapsing forms of MS	Inhibits pyrimidine synthesis/ Immunomodulatory agent	Oral	• NDA filed August 2011 • A response to the NDA is expected June 2012
Teva Pharmaceuticals/ Laquinimod	For the treatment of relapsing-remitting MS	Inhibits autoimmune and inflammatory disease activity/ Immunomodulatory agent	Oral	• Based on guidance from the FDA, Teva will conduct another phase III trial before filing for approval
Neuroendocrine disorders				
Novartis/ Pasireotide (SOM230)	For the treatment of Cushing's disease, carcinoid syndrome and acromegaly	Binds somatostatin receptors/Somatostatin analogue	SC injection	• Designated as an orphan drug • Primary endpoint achieved in phase III acromegaly trial May 2012
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 • NDA filed September 2011 • Received a complete response letter March 2012 • NDA resubmission planned for the first quarter of 2013
Neutropenia				
Teva Pharmaceuticals/ Lipegfilgrastim	To reduce the duration of severe neutropenia in cancer patients undergoing chemotherapy	Long-acting granulocyte colony-stimulating factor	SC injection	• Primary endpoint achieved in phase III trial June 2011 • BLA filing anticipated in 2012

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Oncology				
Agennix/ Talactoferrin	For the third-line treatment of non-small cell lung cancer (NSCLC)	Stimulates immune system to destroy cancer cells/Dendritic cell recruiter and activator	Oral	• Designated as an orphan drug with fast-track status • Results from phase III trial expected in the third quarter of 2012
ARIAD Pharmaceuticals/ Ponatinib	For the treatment of resistant or intolerant chronic myeloid leukemia (CML) or Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Inhibits native and mutant forms of BCR-ABL/ Pan-BCR-ABL inhibitor	Oral	• NDA filing anticipated in the third quarter of 2012
AVEO Pharmaceuticals and Astellas/ Tivozanib	For the treatment of advanced RCC	Reduces tumor cell growth and blood supply/VEGF receptor inhibitor	Oral	• Primary endpoint achieved in phase III trial January 2012 • NDA filing anticipated in the third quarter of 2012
Bayer HealthCare/ Alpharadin (radium-223 chloride)	For the treatment of patients with castrate-resistant prostate cancer (CRPC) and bone metastases	Mimics the behavior of calcium in the bone to target areas of high bone turnover in and around bone metastases/ Alpha-pharmaceutical	IV infusion	• FDA granted fast-track status • Primary endpoint achieved in phase III trial June 2011 • First regulatory submission planned for mid-2012
Bayer HealthCare/ Regorafenib	For the treatment of mCRC and metastatic and/or inoperable gastrointestinal stromal tumors (GIST)	Reduces tumor cell growth and blood supply/Multikinase inhibitor	Oral	• Designated as an orphan drug with fast-track status for GIST • NDA filed for mCRC April 2012
Celgene Corporation/ Pomalidomide	For the treatment of relapsed/refractory multiple myeloma and myelofibrosis	Possesses immunomodulatory, anti-inflammatory and antiangiogenic properties/Thalidomide analogue	Oral	• NDA filed for multiple myeloma in the first quarter of 2012 • Data from phase III trial in myelofibrosis expected by the end of 2012
Cell Therapeutics/ Opaxio™ (paclitaxel poliglumex)	For the treatment of ovarian cancer	Promotes assembly and stabilizes microtubules, resulting in inhibition of cellular division/ Microtubule inhibitor	IV infusion	• Links paclitaxel to a biodegradable polyglutamate polymer that delivers more chemotherapy to tumor cells • Interim analysis of phase III trial may be available in 2013
Cell Therapeutics/ Pixuvri™ (pixantrone)	For the treatment of relapsed or refractory aggressive non-Hodgkin lymphoma	Damages the DNA of cancer cells, resulting in cancer cell death/ Topoisomerase II inhibitor	IV infusion	• Designed to reduce the potential for heart damage, compared with current anthracyclines • Received a complete response letter April 2010 • NDA resubmission planned for 2012

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Oncology				
Eisai/ Lenvatinib	For the treatment of thyroid cancer	Inhibits cell growth and survival/TKI	Oral	• NDA filing planned for 2013
EpiCept/ Ceplene® (histamine dihydrochloride)	In conjunction with interleukin (IL)-2 for remission maintenance in patients with acute myeloid leukemia	Protects the lymphocytes responsible for destroying leukemia cells/Histamine analogue	SC injection	• Designated as an orphan drug • NDA filed June 2010 • Received a refusal to file letter from the FDA August 2010 • Based on feedback from the FDA, EpiCept does not plan to proceed with a phase III trial at this time
Exelixis/ Cabozantinib	For the treatment of medullary thyroid cancer	Inhibits cell growth and survival/TKI	Oral	• Designated as an orphan drug with fast-track status • Rolling NDA submission completed May 2012
Medivation/ Enzalutamide (MDV3100)	For the treatment of advanced prostate cancer after failure of docetaxel-based chemotherapy	Slows cell growth and causes cell death/ Androgen receptor signaling inhibitor	Oral	• FDA granted fast-track status • NDA filed May 2012
Merck/ Taltorvic (ridaforolimus)	For the treatment of metastatic soft tissue or bone sarcomas in patients who had a favorable response to chemotherapy	Inhibits tumor cell growth and the formation of new blood vessels/ mTOR inhibitor	Oral	• Designated as an orphan drug with fast-track status • NDA filed August 2011 • Received a complete response letter June 2012, additional studies are required for approval
Onconova Therapeutics/ Rigosertib	For the treatment of refractory myelodysplastic syndromes	Targets alpha and beta isoforms of PI-3 kinases/ Multikinase inhibitor	IV infusion	• An oral formulation is also in development • NDA filing planned for 2013
Onyx Pharmaceuticals/ Kyprolis™ (carfilzomib)	For the treatment of relapsed and/or refractory multiple myeloma	Causes cell death/ Proteasome inhibitor	IV injection	• Designated as an orphan drug with fast-track status • Rolling NDA completed September 2011 • A response to the NDA is expected July 2012
Pfizer/Bosutinib	For the treatment of previously treated Ph+ CML	Inhibits cell growth and survival/Src and Abl TKI	Oral	• Designated as an orphan drug • NDA filing accepted January 2012
Regeneron Pharmaceuticals and Bayer HealthCare/ Zaltrap™ (aflibercept)	For the treatment of mCRC	Binds VEGF and placental growth factor/ Antiangiogenesis inhibitor	IV infusion	• BLA filed February 2012 • FDA granted priority review status • A response to the BLA is expected August 2012
Teva Pharmaceuticals/ Omapro™ (omacetaxine)	For the treatment of CML in patients who failed treatment with two or more TKIs	Inhibits protein translation of oncoproteins/Cetaxine	SC injection	• Designated as an orphan drug with fast-track status • NDA filing accepted for review May 2012

Pipeline medications in phase III trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Route of administration	Comments
Ophthalmology				
ThromboGenics/ Ocriplasmin	For the treatment of symptomatic vitreomacular adhesion, including macular holes	Targets the fibronectin, laminin and type IV collagen fibers that adhere the vitreous to the retina/Proteolytic enzyme	Intravitreal injection	• BLA resubmitted April 2012
Primary immunodeficiency				
Baxter and Halozyme/HyQvia	Replacement therapy for primary immunodeficiency	Replaces deficient immunoglobulin/ Replacement therapy	SC infusion	• HyQvia contains recombinant human hyaluronidase, which facilitates the dispersion and absorption of the immunoglobulin • BLA filed July 2011 • FDA requested additional information to complete its review of the BLA in April 2012
Biotest/Bivigam™	Replacement therapy for primary immunodeficiency	Replaces deficient immunoglobulin/ Replacement therapy	IV infusion	• BLA filed November 2010 • A response to the BLA is expected in the third quarter of 2012
Pulmonary arterial hypertension				
Actelion/ Macitentan	For the treatment of pulmonary arterial hypertension (PAH)	Reduces vascular smooth muscle constriction/ Endothelin receptor antagonist	Oral	• Primary endpoint achieved in phase III trial April 2012 • NDA filing planned for the fourth quarter of 2012
Short bowel syndrome				
NPS Pharmaceuticals/ Gattex® (teduglutide)	For the treatment of short bowel syndrome by reducing patients' dependence on IV feeding	Promotes gastrointestinal regeneration/Analogue of glucagon-like peptide-2	SC injection	• Designated as an orphan drug • Rolling BLA completed December 2011 • A response to the BLA is expected September 2012
Thrombocytopenia				
Eisai/ Avatrombopag	For the treatment of chronic immune thrombocytopenia	Stimulates platelet production/ Thrombopoietin receptor agonist	Oral	• NDA filing planned for 2013

New dosage forms in the pipeline

Manufacturer/ Drug name	Indication	Mechanism of action/Drug class	Current route of administration	Investigational route of administration*	Comments
Cystic fibrosis					
Novartis/TOBI Podhaler (tobramycin)	For the treatment of *Pseudomonas aeruginosa* infection in cystic fibrosis (CF) patients	Disrupts protein synthesis/ Aminoglycoside antibiotic	Solution for inhalation	Powder for inhalation	• NDA filed December 2011 • A response to the NDA is expected October 2012
Pharmaxis/ Bronchitol (mannitol)	For the treatment of CF	Hydrates the lungs/Osmotic diuretic	IV infusion, inhalation	Inhalation	• Designated as an orphan drug • NDA filed May 2012
Lysosomal storage diseases					
Raptor Pharmaceutical/ RP103 (cysteamine bitartrate delayed-release)	For the treatment of nephropathic cystinosis	Reduces cystine levels in cells/ Aminothiol	Oral	Oral	• Formulated to be sprinkled onto food for administration • Designated as an orphan drug • NDA filed March 2012
Multiple sclerosis					
Biogen Idec and Abbott/ 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 trial currently enrolling participants • Marketed as Zenapax® for the prevention of acute kidney rejection
Oncology					
Genentech/ Trastuzumab emtansine	For the treatment of HER2-positive metastatic breast cancer	Inhibits the proliferation of tumor cells that overexpress HER2/Antibody-drug conjugate	IV infusion	IV infusion	• Links trastuzumab antibody to anti-cancer agent • BLA filing planned for 2012
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 • Two additional studies are currently ongoing
Talon Therapeutics/ Marqibo® (vincristine sulfate in liposomes)	For the treatment of relapsed or refractory ALL	Inhibits microtubule formation/Vinca alkaloid	IV infusion	IV infusion	• Encapsulated formulation of vincristine • NDA filed July 2011 • A response to the NDA was expected May 2012; however, the FDA has extended the review period • A response is now expected August 2012
Pulmonary arterial hypertension					
United Therapeutics/ Treprostinil diethanolamine	For the treatment of PAH	Dilates pulmonary blood vessels/ Prostacyclin analogue	Continuous SC or IV infusion and inhalation	Oral	• NDA filing accepted February 2012 • A response to the NDA is expected October 2012

New indications in the pipeline

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/Drug class	Route of administration	Comments
Human immunodeficiency virus					
Gilead Sciences/ Truvada® (emtricitabine, tenofovir)	In combination with other antiretroviral agents for the treatment of HIV-1 infection	For pre-exposure prophylaxis to reduce the risk of HIV-1 infection among uninfected adults	Inhibits viral replication/ Reverse transcriptase inhibitor	Oral	• Supplemental new drug application (sNDA) filing accepted February 2012 • FDA granted priority review status • A response to the sNDA was expected June 2012; however, the FDA has extended the review period • A response is now expected September 2012
Inflammatory diseases					
Abbott/ Humira® (adalimumab)	For the treatment of RA, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease and plaque psoriasis	For the treatment of moderate to severe ulcerative colitis	Targets tumor necrosis factor (TNF) alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	• Supplemental biologics license application (sBLA) filed in 2011 • Received a complete response letter in late 2011 • Abbott has submitted additional information to the FDA
Novartis/Ilaris® (canakinumab)	For the treatment of cryopyrin-associated periodic syndromes (CAPS)	For the treatment of refractory acute gout flares and systemic juvenile idiopathic arthritis (SJIA)	Targets IL-1 beta/IL-1 beta inhibitor	SC injection	• sBLA filed for gout in the first quarter of 2011 • Received a complete response letter August 2011 • Novartis is working with the FDA to determine next steps in gout • sBLA filing for SJIA planned for 2012
Regeneron Pharmaceuticals/ Arcalyst® (rilonacept)	For the treatment of CAPS, including familial cold auto-inflammatory syndrome and Muckle-Wells syndrome	For the prevention of gout flares in patients initiating uric acid-lowering therapy	Binds and neutralizes IL-1/ Long-acting IL-1 inhibitor	SC injection	• sBLA filed September 2011 • A response to the sBLA is expected July 2012
Genentech/ Actemra® (tocilizumab)	For the treatment of RA and SJIA	For the treatment of polyarticular juvenile idiopathic arthritis	Blocks IL-6 receptors/ Monoclonal antibody	IV infusion	• Phase III trial met primary endpoint April 2012
UCB Pharma/ Cimzia® (certolizumab pegol)	For the treatment of Crohn's disease and RA	For the treatment of psoriatic arthritis	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	• sBLA filing anticipated by the end of 2012

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 chronic lymphocytic leukemia (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 • Marketed as Campath® for CLL indication
Neuropathy					
Baxter/ Gammagard Liquid (immune globulin, human)	For replacement therapy in primary humoral immunodeficiency	For the treatment of multifocal motor neuropathy	Replaces immune globulin G (IgG) antibodies/ Highly purified and concentrated IgG antibodies	IV infusion	• sBLA filed January 2012 • A response to the sBLA is expected November 2012
Oncology					
Amgen/ Xgeva® (denosumab)	For the prevention of skeletal-related events in patients with bone metastases from solid tumors	For the treatment of men with CRPC to reduce the risk of bone metastases	Inhibits bone destruction/ Receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor	SC injection	• sBLA filed June 2011 • Received a complete response letter April 2012; the FDA requested additional data
Celgene/ Abraxane® (paclitaxel protein-bound particle)	For the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy	For the treatment of NSCLC	Promotes assembly and stabilizes microtubules, resulting in inhibition of cellular division/ Microtubule inhibitor	IV infusion	• sNDA filed December 2011 • A response to the sNDA is expected October 2012
GlaxoSmithKline/ Tykerb® (lapatinib)	In combination with Xeloda® (capecitabine) or Femara® (letrozole) for the treatment of breast cancer	In combination with Herceptin® (trastuzumab) for the treatment of patients with HER2-positive metastatic breast cancer who have received prior Herceptin therapy	Inhibits cell growth and survival/TKI	Oral	• sNDA filed February 2012

New indications in the pipeline (continued)

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/Drug class	Route of administration	Comments
Oncology					
Johnson & Johnson/ Zytiga® (abiraterone acetate)	For the treatment of patients with metastatic CRPC who have received prior chemotherapy containing docetaxel	For the treatment of patients with metastatic CRPC who are asymptomatic or mildly symptomatic and have not received chemotherapy	Suppresses testosterone production/ Androgen biosynthesis inhibitor	Oral	• sNDA filed June 2012
Novartis/ Afinitor® (everolimus)	For the treatment of advanced RCC, progressive neuroendocrine tumors of pancreatic origin, subependymal giant cell astrocytoma associated with TSC and renal angiomyolipoma associated with TSC	In combination with Aromasin® (exemestane) for the treatment of estrogen receptor-positive (ER+) HER2-breast cancer	Inhibits tumor cell growth and the formation of new blood vessels/mTOR inhibitor	Oral	• sNDA for breast cancer filed at the end of 2011
Novartis/ Tasigna® (nilotinib)	For the treatment of chronic and accelerated-phase Ph+ CML in patients resistant or intolerant to prior therapy that included Gleevec, and for the first-line treatment of Ph+ CML	For the treatment of c-Kit-positive melanoma	Inhibits cell growth and survival/TKI	Oral	• sNDA planned for 2014
Ophthalmology					
Regeneron Pharmaceuticals/ Eylea® (aflibercept)	For the treatment of neovascular age-related macular degeneration	For the treatment of central retinal vein occlusion	Binds VEGF and placental growth factor/ Antiangio-genesis inhibitor	Intravitreal injection	• sBLA filed in November 2011 • A response to the sBLA is expected September 2012
Peyronie's Disease					
Auxilium Pharmaceuticals/ Xiaflex® (collagenase clostridium histolyticum)	For the treatment of Dupuytren's contracture with a palpable cord	For the treatment of Peyronie's disease	Breaks down collagen deposits/ Purified collagenase	Injection	• sBLA filing planned for 2012

New indications in the pipeline (continued)

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/Drug class	Route of administration	Comments
Pulmonary arterial hypertension					
Novartis/ Gleevec® (imatinib)	For the treatment of CML, ALL, myelodysplastic/ myeloproliferative diseases, aggressive systemic mastocytosis, hypereosinophilic syndrome, chronic eosinophilic leukemia, dermato-fibrosarcoma protuberans and GIST	For the treatment of PAH	Improves pulmonary vascular resistance and increases cardiac output/TKI	Oral	• sNDA filed in February 2012
Thrombocytopenia					
GlaxoSmithKline/ Promacta® (eltrombopag)	For the treatment of thrombocytopenia in patients with chronic HCV infection to enable the initiation of interferon-based therapy and to optimize interferon-based therapy	For the treatment of chronic immune thrombocyto-penia	Stimulates platelet production/ Thrombopoietin receptor agonist	Oral	• sNDA filed May 2012 • A response to the sNDA is expected March 2013

Glossary of terms

Accelerated approval – allows pharmaceutical companies to obtain approval for products based on less clinical data than typically required for a normal approval, and is used for patients considered to have unmet medical needs.

Approvable letter – term used when assessing NDAs which indicated that a medication could probably be approved at a later date, provided that the applicant supplied requested information to the FDA or made specified changes. Since Aug. 11, 2008, the FDA has issued a complete response letter to the applicant in place of an approvable letter.

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

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.

Cystic fibrosis – CF.

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.

Expanded access program – manufacturer programs that allow the distribution of new medications prior to FDA approval for patients with a life-threatening condition who cannot be treated successfully with currently available medications.

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.

Hereditary angioedema – HAE.

Multiple sclerosis – MS.

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.

Nonapprovable letter – term used when assessing NDAs which indicated the application had deficiencies that generally required the submission of substantial data before the application could be approved. Since Aug. 11, 2008, the FDA has issued a complete response letter to the applicant in place of a nonapprovable letter.

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 II – second phase of medication development; typically involves several hundred patients to determine safety and preliminary data on efficacy.

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.

Pulmonary arterial hypertension – PAH.

Randomized controlled trial – a study in which people are allocated at random (by chance alone) to receive one of several clinical interventions. It is the most powerful study design in clinical research.

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

Rheumatoid arthritis – RA.

Risk evaluation and mitigation strategy (REMS) – a strategy to manage a known or potential serious risk associated with a drug or biological product. This strategy will be required if the FDA finds that a REMS is necessary to ensure that the benefits of the drug or biological product outweigh its risks.

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.

References

Journals:

Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients. *J Clin Lipidol*. 2011;5:S1-S8.

Grothey A. Advances in oncology: CRC in focus: regorafenib in metastatic colorectal cancer. *Clin Adv Hematol Oncol*. 2012;10:324-325.

Motzer RJ, Nosov D, Eisen T, et al. Tivozanib versus sorafenib as initial targeted therapy for patients with advanced renal cell carcinoma: results from a phase III randomized, open-label, multicenter trial. *J Clin Oncol*. 2012;suppl:abstract 4501.

National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. National Heart, Lung, and Blood Institute website. http://www.nhlbi.nih.gov/guidelines/cvd_ped/peds_guidelines_full.pdf. Accessed June 12, 2012.

Parhofer KG. Mipomersen: evidence-based review of its potential in the treatment of homozygous and severe heterozygous familial hypercholesterolemia. *Core Evid*. 2012;7:29-38.

Van Cutsem E, Sobrero AF, Siena S, et al. Phase III CORRECT trial of regorafenib in metastatic colorectal cancer (mCRC). *J Clin Oncol*. 2012;suppl:abstract 3502.

Websites:

Inteleos™- www.inteleos.com/inteleos.html

Manufacturers' websites

ClinicalTrials.gov - www.clinicaltrials.gov

U.S. Food and Drug Administration - www.fda.gov

Information in the report is current as of June 2012, and was accessed on June 18, 2012.

This report is for educational purposes only and is not deemed as an endorsement by Walgreen Co., its subsidiaries or affiliates. Claims made in this report about the efficacy of medications or the results of studies have been made by the medication manufacturer, the FDA or another third party.

Drug names are the property of their respective owners.

Editorial Board - Editor Stacy Goldman **Author** Amy Pfeifer, PharmD **Project Lead** Tim Kosmaczewski **Designer** Edmond He