



Specialty Pharmacy Pipeline Report

Second Quarter 2009

To help keep you informed about medications in development, the *Walgreens Specialty Pharmacy 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, newly 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.

Trabectedin

Ortho Biotech filed a new drug application (NDA) in November 2008 for trabectedin to be used in combination with Doxil® (doxorubicin) for the treatment of relapsed ovarian cancer. According to the American Cancer Society, approximately 21,550 new cases of ovarian cancer and 14,600 deaths will occur this year.

Trabectedin is a non-platinum antitumor agent that interferes with cell division, genetic transcription processes and DNA repair machinery. In clinical trials, trabectedin was administered as an intravenous (IV) infusion over three hours every three weeks at a dose of 1.1 mg/m². In a phase III study, patients were randomized to receive Doxil (30mg/m²) followed by trabectedin or Doxil (50 mg/m² every four weeks) alone. The patients receiving a combination of Doxil

and trabectedin had a longer progression-free survival (PFS) compared with those receiving Doxil alone (7.3 months versus 5.8 months, respectively). The difference in PFS between the groups was statistically significant.

Patients in the trabectedin and Doxil combination group experienced more hematological and gastrointestinal adverse reactions, as well as liver enzyme elevations compared with the patients receiving Doxil alone. Alternatively, patients receiving Doxil alone experienced more commonly associated Doxil adverse events, such as hand-foot syndrome and stomatitis compared with the combination group. Ortho Biotech expects a response to its NDA in September 2009.

Pirfenidone

InterMune has developed pirfenidone for the treatment of idiopathic pulmonary fibrosis (IPF). IPF is a progressive condition characterized by the formation of scar tissue within the lungs. Currently, there are no FDA approved treatments and median survival is only two to five years from the time of diagnosis. The mainstay of therapy is prednisone combined with either azathioprine or cyclophosphamide; however, lung transplantation has been the only treatment that has been shown to prolong survival.

Pirfenidone is an oral antifibrotic agent that suppresses the production of inflammatory cytokines. In two phase III studies, the efficacy of pirfenidone (801 mg three times a day) in IPF patients with mild to moderate lung function impairment was compared to placebo. The primary endpoint of both studies was change in percent

predicted forced vital capacity after 72 weeks of treatment. The second trial met the primary endpoint, while the first trial did not. The most common adverse events in the pirfenidone groups were nausea, rash, fatigue, diarrhea, dyspepsia and dizziness. InterMune plans to submit an NDA for pirfenidone this year.

Boceprevir and Telaprevir

Boceprevir and telaprevir are investigational agents for the treatment of chronic hepatitis C virus (HCV) infection in treatment-naïve and treatment-failure patients. The CDC estimates that there are 3.2 million Americans chronically infected with HCV infection. Chronic infection with HCV can lead to liver cirrhosis, liver cancer and liver failure. HCV is the most common indication for liver transplantation in the United States.

The current standard of treatment for chronic HCV infection is the use of a pegylated interferon alfa in combination with ribavirin. Boceprevir and telaprevir are both oral protease inhibitors, which prevent HCV replication. They are each being studied as part of a triple medication regimen in combination with a pegylated interferon alfa and ribavirin.

Boceprevir was developed by Schering-Plough, the manufacturer of two current HCV treatments, Peg-Intron™ (peginterferon alfa-2b) and Rebetol® (ribavirin). A phase II study examined the use of boceprevir in treatment-naïve genotype 1 HCV patients. In this study, the sustained virologic response (SVR) rates were 75 percent in the patients who received four weeks of Peg-Intron and Rebetol followed by the addition of boceprevir (800 mg three times a day) for 44 weeks. In comparison, the control group receiving Peg-Intron and Rebetol for 48 weeks achieved SVR rates of 38 percent.

In January 2009, the company completed enrollment of boceprevir phase III registration studies, which are expected to be completed by mid-2010. These studies will evaluate the efficacy of boceprevir in combination with Peg-Intron and Rebetol compared to a control of Peg-Intron and Rebetol in treatment-naïve and treatment-failure patients with chronic genotype 1 HCV.

Telaprevir was developed by Vertex Pharmaceuticals and has been studied in combination with Roche's HCV treatments, Pegasys® (peginterferon alfa-2a) and Copegus® (ribavirin). The company completed two

phase II studies in treatment-naïve genotype 1 HCV patients and one phase II study in treatment-failure genotype 1 HCV patients. In the treatment-naïve studies, patients in the groups receiving 12 weeks of telaprevir in combination with Pegasys and Copegus followed by an additional 12 weeks of Pegasys and Copegus alone achieved SVR rates of 61 percent and 69 percent. In these studies, the control groups received 48 weeks of treatment with Pegasys and Copegus and achieved SVR rates of 41 percent and 46 percent.

In the treatment-failure trial, patients receiving 12 weeks of telaprevir in combination with Pegasys and Copegus followed by an additional 12 weeks of Pegasys and Copegus alone achieved SVR rates of 51 percent. In comparison, the control group receiving Pegasys and Copegus for 48 weeks achieved SVR rates of 14 percent.

Vertex completed enrollment for the telaprevir phase III registration studies in February 2009. These studies will evaluate the efficacy of telaprevir in combination with Pegasys and Copegus compared to a control of Pegasys and Copegus in treatment-naïve and treatment-failure patients with chronic genotype 1 HCV. If successful, the company expects to file for telaprevir's approval in the second half of 2010.

Medications Recently Approved

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Approval Date	Comments
Inflammatory Diseases					
Centocor and Schering-Plough/ Simponi™ (golimumab)	For the treatment of rheumatoid arthritis (RA), psoriatic arthritis and ankylosing spondylitis	Targets tumor necrosis factor (TNF) alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	04/24/2009	Simponi is a self-administered TNF inhibitor with once-monthly dosing.
UCB/ Cimzia® (certolizumab pegol)	For the treatment of moderately to severely active RA	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	05/14/2009	Previously approved for the treatment of Crohn's disease.
Oncology					
Genentech/ Avastin® (bevacizumab)	For the treatment of glioblastoma in patients with progressive disease following a prior therapy	Binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF)/ Anti-angiogenesis agent	IV infusion	05/06/2009	Previously approved for the treatment of breast cancer, colorectal cancer and non-small cell lung cancer (NSCLC).
Novartis/ Afinitor® (everolimus, RAD001)	For the treatment of advanced renal cell carcinoma (RCC) in patients who have failed treatment with Sutent® or Nexavar®	Inhibits tumor cell growth and the formation of new blood vessels/ Mammalian target of rapamycin (mTOR) inhibitor	Oral	03/30/2009	First medication approved in this patient population.
Schering-Plough/ Temodar® (temozolomide)	For the treatment of newly diagnosed glioblastoma and refractory anaplastic astrocytoma	Causes cell death and disrupts cell division/ Alkylating agent	IV infusion	02/27/2009	This is a new injectable formulation. Temodar capsules were approved in 1999.
Osteoarthritis					
Genzyme/ Synvisc-One™ (hylan G-F 20)	For the treatment of pain in osteoarthritis of the knee	Supplements or replaces synovial fluid/Viscosupplement	Intra-articular (IA) injection	02/26/2009	Synvisc-One is administered as a single IA injection. It is an alternative to other viscosupplements that require three to five injections.

Pipeline Medications in Phase III Trials

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Amyloid A Amyloidosis				
BELLUS Health/ Kiacta™ (eprodisate), formerly Fibrillex™	For the treatment of amyloid A amyloidosis	Reduces amyloid protein deposition/ Amyloid fibrillogenesis inhibitor	Oral	Designated as an orphan drug. NDA filed February 2006. FDA granted priority review status April 2006. First approvable letter August 2006. Second approvable letter July 2007. NDA withdrawn March 2008. A second phase III trial was submitted for a special protocol assessment (SPA).
Anemia				
Affymax and Takeda/ Hematide™	For the treatment of anemia in patients with chronic renal failure	Binds to and activates the erythropoietin receptor/Erythropoiesis stimulating agent	Injection	Administered once every four weeks in clinical trials. NDA filing planned for 2010.
Blood Disorder				
GlaxoSmithKline/ Bosatria® (mepolizumab)	For the treatment of hypereosinophilic syndrome	Binds to and inactivates interleukin (IL)5/Anti-IL- 5 monoclonal antibody	IV infusion	Designated as an orphan drug. BLA filing was expected in 2008; however, GlaxoSmithKline is now reviewing its filing strategy.
Cystic Fibrosis				
Inspire Pharmaceuticals/ Denufosal	For the treatment of cystic fibrosis	Designed to enhance mucosal hydration and mucociliary clearance/Second generation P2Y ₂ agonist	Inhalation	Designated as an orphan drug with fast track status. Second phase III study initiated February 2008. Primary endpoint achieved in first phase III trial June 2008.
Gaucher Disease				
Protalix/ prGCD (plant cell expressed recombinant glucocerebrosidase)	For the treatment of Gaucher disease	Replaces deficient glucocerebrosidase/ Enzyme replacement therapy	IV infusion	Enrollment completed for the pivotal phase III trial, which is being conducted under an SPA December 2008. NDA filing anticipated fourth quarter 2009.
Shire/ Velaglycerase alfa	For the treatment of type 1 Gaucher disease	Replaces deficient glucocerebrosidase/ Enzyme replacement therapy	IV infusion	Worldwide enrollment completed for phase III clinical program July 2008. BLA filing anticipated second half 2009.
Hepatitis				
Human Genome Sciences and Novartis/ Albuzeron® (albinterferon alfa-2b)	In combination with ribavirin for the treatment of HCV infection	Inhibits viral replication/Interferon	Injection	Primary endpoint achieved in two pivotal phase III trials April 2009. BLA filing anticipated by fall 2009.
Schering-Plough/ Boceprevir	In combination with Peg-Intron (peginterferon alfa- 2b) and Rebetol (ribavirin) for the treatment of chronic HCV infection in treatment-naïve and treatment- failure patients	Prevents virus replication/Protease inhibitor	Oral	Enrollment completed for phase III registration studies January 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Hepatitis				
Vertex Pharmaceuticals/ Telaprevir	In combination with peginterferon and ribavirin for the treatment of chronic HCV infection in treatment-naïve and treatment-failure patients	Prevents virus replication/Protease inhibitor	Oral	Enrollment completed for phase III registration studies February 2009.
Hereditary Angioedema				
CSL Behring/ Berinert® P (C1 inhibitor)	For the treatment of acute attacks in patients with hereditary angioedema (HAE)	Replaces deficient C1 inhibitor/C1 inhibitor replacement therapy	IV infusion	Designated as an orphan drug. BLA filed March 2008. A response to the BLA was expected January 2009. In February, CSL Behring reported that they were addressing questions raised by the FDA related to the drug's manufacturing process and clinical data.
Dyax/ Kalbitor (ecallantide, DX-88)	For the treatment of moderate to severe acute HAE attacks	Inhibits the release of bradykinin, thereby preventing swelling and pain associated with HAE attacks/ Recombinant plasma kallikrein inhibitor	SC injection	Designated as an orphan drug with fast track status. BLA filed September 2008. FDA granted priority review status November 2008. Complete response letter March 2009. No new clinical studies are required, but the FDA has requested additional information, including a proposal for a Risk Evaluation and Mitigation Strategy (REMS).
Pharming Group NV/ Rhucin® (C1 inhibitor)	For the treatment of acute attacks in patients with HAE	Replaces deficient C1 inhibitor/C1 inhibitor replacement therapy	IV infusion	Designated as an orphan drug. BLA filed December 2008, but was transferred to another division of the FDA. Pharming plans to resubmit its BLA in 2009.
Human Immunodeficiency Virus (HIV)				
Schering-Plough/ Vicriviroc	For the treatment of R5-type HIV infection in combination with other antiretroviral agents (which must include a protease inhibitor) in treatment-experienced patients	Inhibits entry of virus into human CD4 T-cells/Cellular chemokine receptor antagonist (CCR-5)	Oral	Initiated two large phase III trials September 2007.
Theratechnologies/ Tesamorelin	For the treatment of HIV-associated lipodystrophy	Reduces visceral adipose tissue/Growth hormone-releasing factor analogue	SC injection	NDA filing planned for 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Infertility				
Schering-Plough/ 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	Primary endpoints in phase III trial were met July 2008.
Inflammatory Diseases				
Centocor/ Stelara (ustekinumab)	For the treatment of adult patients with chronic moderate to severe plaque psoriasis	Targets IL-12 and IL-23/ Dual IL inhibitor	SC injection	BLA filed December 2007. Complete response letter December 2008. No new clinical studies are required, but the FDA has requested additional information, including a proposal for a REMS.
Novartis/ Canakinumab (ACZ885)	For the treatment of cryopyrin-associated periodic syndromes, including Muckle-Wells syndrome	Targets IL-1 β / IL-1 β inhibitor	SC injection	Designated as an orphan drug. BLA filed December 2008. A response to the BLA is expected October 2009.
Roche/ Actemra™ (tocilizumab)	For reducing the signs and symptoms in adults with moderate to severe RA	Blocks IL-6 receptors/ Monoclonal antibody	IV infusion	BLA filed November 2007. Complete response letter September 2008. No new clinical studies are required, but the FDA has requested additional information, including a proposal for a REMS.
Savient Pharmaceuticals/ Krystexxa (pegloticase)	For the treatment of gout in patients for whom conventional treatment is contraindicated or ineffective	Lowers the plasma level of uric acid/ Bio-uricolytic agent	IV infusion	Designated as an orphan drug. BLA filed October 2008. FDA granted priority review status December 2008. A response to the BLA was expected April 2009; however, Savient filed amendments to its BLA resulting in a three-month extension to the review period. A response to the BLA is now expected July 2009.
Multiple Sclerosis				
Acorda Therapeutics/ Fampridine-SR	To improve walking ability in patients with multiple sclerosis (MS)	Improves impulse conduction in nerve fibers with damaged myelin/ Selective neuronal potassium channel blocker	Oral	Designated as an orphan drug. NDA originally filed January 2009, then resubmitted April 2009. FDA granted priority review status May 2009. A response to the NDA is expected October 2009.
Eli Lilly and BioMS Medical/ Dirucotide (MBP8298)	For the treatment of secondary-progressive MS	Induction or restoration of immunological tolerance/ Synthetic human myelin basic protein	IV infusion	Patient enrollment for phase III trial completed August 2008. FDA granted fast track status.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Multiple Sclerosis				
Novartis/ Fingolimod (FTY720)	For the treatment of relapsing-remitting MS	Reduces inflammation and myelin damage in the brain and spinal cord/ Immuno-modulatory agent	Oral	NDA filing planned for end of 2009.
Sanofi-aventis/ Teriflunomide	For the treatment of relapsing forms of MS	Inhibits pyrimidine synthesis/Immuno-modulatory agent	Oral	Also being studied in combination with interferon-beta and with Copaxone® (glatiramer acetate).
Teva/ Laquinimod	For the treatment of relapsing-remitting MS	Inhibits autoimmune and inflammatory disease activity/ Immunomodulatory agent	Oral	Patient enrollment for phase III trial completed November 2008.
Neuroendocrine Disorders				
Novartis/ Pasireotide	For the treatment of Cushing's disease and acromegaly	Binds somatostatin receptors/Somatostatin analogue	SC injection	NDA filing for Cushing's disease planned for 2010.
Oncology				
AstraZeneca/ Zactima® (vandetanib)	For the second-line treatment of NSCLC	Reduces tumor cell growth and blood supply/Multikinase inhibitor	Oral	NDA filing planned for first half of 2009.
Cell Therapeutics/ Opaxio™ (paclitaxel poliglumex), formerly Xyotax™	For the treatment of advanced NSCLC in women and for maintenance treatment of ovarian cancer	Promotes assembly and stabilizes microtubules resulting in inhibition of cellular division/ Antimicrotubule chemotherapy agent	IV infusion	Links paclitaxel to a biodegradable polyglutamate polymer that delivers more chemotherapy to tumor cells. Received SPA approval from the FDA for phase III trial in NSCLC September 2007. FDA granted fast track status.
Allos Therapeutics/ Pralatrexate	For the treatment of relapsed or refractory peripheral T-cell lymphoma	Interferes with DNA synthesis and triggers cancer cell death/ Antifolate	IV injection	NDA filed March 2009. A response to the NDA is expected January 2010.
Cell Therapeutics/ Pixantrone	For the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma (NHL)	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 to current anthracyclines. Rolling NDA submission initiated April 2009.
Cephalon/ Lestaurtinib	For the treatment of acute myeloid leukemia (AML)	Inhibits FMS-like tyrosine kinase-3 (FLT3) mutations/ FLT3 inhibitor	Oral	Designated as an orphan drug. NDA filing planned for 2009.
Dendreon/ Provenge® (sipuleucel-T)	For the treatment of metastatic hormone-refractory prostate cancer (HRPC)	Stimulates immune system to target and destroy cancer cells/Active cellular immunotherapy	IV infusion	BLA filed November 2006. Complete response letter May 2007. Dendreon plans to file an amendment to its existing BLA in the fourth quarter of 2009.
EpiCept/ Ceplene® (histamine dihydrochloride)	In conjunction with IL-2 as a remission maintenance treatment of AML	Protects the lymphocytes responsible for destroying leukemia cells/Histamine analogue	SC injection	Designated as an orphan drug. NDA filing planned for second half 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
Genmab and GlaxoSmithKline/ Arzerra™ (ofatumumab)	For the treatment of refractory chronic lymphocytic leukemia (CLL)	Targets the binding site of CD20 on B-cells/Anti- CD20 monoclonal antibody	IV infusion	BLA filed January 2009. FDA granted priority review status April 2009. A response to the BLA is expected July 2009.
Genta/ Genasense® (oblimersen)	For the treatment of relapsed or refractory CLL in combination with chemotherapy	Inhibits the production of Bcl-2/Antisense therapy	IV infusion	Designated as an orphan drug. NDA filed December 2005. Non-approvable letter December 2006. NDA amended June 2008. Complete response letter December 2008. The FDA has requested an additional clinical trial to confirm efficacy.
Marshall Edwards/ Phenoxodiol	For the treatment of HRPC in Taxotere® (docetaxel) nonresponders and recurrent chemotherapy- resistant, late-stage ovarian cancer	Causes cell death through inhibition of antiapoptotic proteins/ Antineoplastic (multiple signal transduction regulator)	IV injection/Oral	Received SPA approval from the FDA for phase III trial in ovarian cancer. FDA granted fast track status.
Merck and Ariad Pharmaceuticals/ Deforolimus (MK-8669)	For the treatment of metastatic sarcoma	Inhibits tumor cell growth and the formation of new blood vessels/mTOR inhibitor	Oral	NDA filing planned for 2010.
Ortho Biotech/ Trabectedin	In combination with Doxil® (doxorubicin) for the treatment of relapsed ovarian cancer	Interferes with cell division, genetic transcription processes and DNA repair machinery/Non- platinum antitumor agent	IV infusion	NDA filed November 2008. A response to the NDA is expected September 2009.
Sanofi-aventis/ Larotaxel	For second-line treatment of pancreatic cancer	Inhibits the growth and development of cancer cells/Taxane derivative	IV infusion	NDA filing planned for June 2010.
Vion Pharmaceuticals/ Onrigin (laromustine)	For remission induction in patients 60 years or older with <i>de novo</i> poor-risk AML	Causes cell death and disrupts cell division/ Alkylating agent	IV infusion	NDA filed February 2009. A response to the NDA is expected December 2009.
Osteoporosis				
Amgen/ Denosumab	For the treatment of postmenopausal osteoporosis (PMO) and cancer- related bone loss	Inhibits bone destruction/ Monoclonal antibody	SC injection	BLA filed for PMO and cancer-related bone loss December 2008. A response to the BLA is expected October 2009.
Primary Immunodeficiencies				
CSL Behring/ Immune globulin with proline	For the treatment of primary immunodeficiencies	Replaces deficient immune globulin/ Replacement therapy	SC infusion	BLA filed May 2009. A response to the BLA is expected March 2010.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Pulmonary Arterial Hypertension				
Pfizer/ Theelin™ (sitaxsentan)	For the treatment of pulmonary arterial hypertension (PAH)	Reduces vascular smooth muscle constriction/ Endothelin receptor antagonist	Oral	Designated as an orphan drug. NDA filed May 2005. First approvable letter March 2006. Second approvable letter July 2006. Third approvable letter June 2007. Phase III study initiated November 2008.
Pulmonary Fibrosis				
InterMune/ Pirfenidone	For the treatment of idiopathic pulmonary fibrosis (IPF)	Suppresses the production of inflammatory cytokines/Antifibrotic agent	Oral	Currently, there are no FDA approved treatments for IPF. Designated as an orphan drug. NDA filing planned for 2009.
Respiratory Syncytial Virus				
MedImmune and AstraZeneca/ Numax® (motavizumab)	For the prevention of respiratory syncytial virus (RSV) infection in high-risk pediatric populations	Inhibits RSV replication/ Monoclonal antibody	IM injection	Expected to be more potent than Synagis® (palivizumab), the current standard of care for the prevention of RSV. BLA filed January 2008. Complete response letter November 2008. The FDA has requested additional information.

New Dosage Forms in the Pipeline

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Current Route of Administration	Investigational Route of Administration*	Comments
Acromegaly					
Ambrilia/ C2L (octreotide)	For the treatment of acromegaly	Binds somatostatin receptors/ Somatostatin analogue	IM injection	IM injection	C2L is a prolonged-release formulation of octreotide designed to be dosed less frequently than the long-acting release formulation—Sandostatin LAR®. NDA filing planned for the first half 2009.
Cystic Fibrosis					
Gilead Sciences/ Cayston™ (aztreonam lysine)	For the treatment of patients with cystic fibrosis who have pulmonary <i>Pseudomonas aeruginosa</i>	Inhibits bacterial cell wall synthesis/ Monobactam antibiotic	IV injection	Inhalation	Designated as an orphan drug. NDA filed November 2007. Complete response letter September 2008. Gilead appealed this decision; however, the FDA reiterated its position and the need for Gilead to conduct an additional clinical study before the NDA can be resubmitted. Available through an expanded access program.

New Dosage Forms in the Pipeline (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Current Route of Administration	Investigational Route of Administration*	Comments
Cystic Fibrosis					
Novartis/ TBM100 (tobramycin)	For the treatment of patients with cystic fibrosis who have pulmonary <i>Pseudomonas aeruginosa</i>	Disrupts protein synthesis/ Aminoglycoside antibiotic	Solution for inhalation	Powder for inhalation	Expected to provide more rapid and convenient administration of tobramycin. NDA filing planned for 2009.
Multiple Sclerosis					
Merck Serono and Teva/ Mylinax® (oral cladribine)	For the treatment of relapsing forms of MS	Interferes with lymphocytes, which are involved in the pathology of MS/ Antineoplastic (purine nucleoside analogue)	IV infusion	Oral	Designated as an orphan drug with fast track status. NDA filing planned for mid-2009.
Oncology					
Watson Pharmaceuticals/ Trelstar® (triptorelin pamoate)	For the palliative treatment of advanced prostate cancer	Suppresses the production of testosterone/ Luteinizing hormone-releasing hormone agonist	IM injection	IM injection	A sustained-release formulation designed to be administered every six months. NDA filed September 2008. A response to the NDA is expected July 2009.
Pulmonary Arterial Hypertension					
United Therapeutics and Lung Rx/ Tyvaso (treprostinil), formerly Viveta	For the treatment of PAH	Dilates pulmonary blood vessels/ Prostacyclin analogue	SC or IV infusion	Inhalation	Studied in combination with Tracleer® (bosentan) or Revatio® (sildenafil). NDA filed June 2008. United Therapeutics amended the NDA in April 2009. A response to the NDA is now expected July 2009.

*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
Asthma					
Genentech/ Xolair® (omalizumab)	For the treatment of adults and adolescents (12 years of age and above) with moderate to severe persistent allergic asthma	For the treatment of children (6 years of age and above) with moderate to severe persistent allergic asthma	Decreases the release of allergic mediators/ Antiimmunoglobulin E agent	SC injection	Supplemental biologic license application (sBLA) filed December 2008. A response to the sBLA is expected October 2009.

New Indications in the Pipeline (continued)

Manufacturer/ Drug Name	Current Indication	Investigational Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Hereditary Angioedema					
ViroPharma / Cinryze™ (C1 inhibitor)	For routine prophylaxis against angioedema attacks in patients with HAE	For the treatment of acute angioedema attacks in patients with HAE	Replaces deficient C1 inhibitor/C1 inhibitor replacement therapy	IV infusion	sBLA filed December 2008. FDA granted priority review status February 2009. A response to the sBLA is expected June 2009.
Human Immunodeficiency Virus (HIV)					
Merck/ Isentress® (raltegravir)	In combination with other antiretroviral agents for treatment-experienced HIV patients who have evidence of viral replication and HIV strains resistant to multiple anti-retroviral agents	In combination with other antiretroviral agents for patients with treatment-naïve HIV	Inhibits the insertion of the HIV viral DNA into human DNA/ Integrase inhibitor	Oral	Supplemental new drug application (sNDA) filed September 2008. A response to the sNDA is expected July 2009.
Infantile Spasms					
Questcor Pharmaceuticals/ H.P. Acthar® Gel (repository corticotrophin injection)	Multiple indications, including the diagnostic testing of adrenocortical function and the treatment of MS exacerbations	For the treatment of infantile spasms	Stimulates the adrenal cortex to secrete cortisol/ Highly purified preparation of adrenocorticotrophic hormone	IM or SC injection	sNDA filed June 2006. Not approvable letter May 2007. sNDA resubmitted December 2008. The filing required reformatting and was completed March 2009.
Inflammatory Diseases					
Bristol-Myers Squibb/ Orencia® (abatacept)	For the treatment of moderately to severely active RA in adults For the treatment of moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 6 years of age and older	For the treatment of patients with early RA	Inhibits T-cell activation/Selective costimulation modulator	IV infusion	sNDA filed in the fourth quarter 2008.
Genentech and Biogen Idec/ Rituxan® (rituximab)	For the treatment of NHL For the treatment of moderately to severely active RA in patients who have had an inadequate response to one or more TNF inhibitors	For the treatment of moderately to severely active RA in patients who have had an inadequate response to prior treatment with a disease modifying anti-rheumatic drug	Reduces the amount of CD20-positive B-cells in the blood/Therapeutic antibody	IV infusion	sBLA filed October 2008.

New Indications in the Pipeline (continued)

Manufacturer/ Drug Name	Current Indication	Investigational Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology					
Genentech/ Avastin® (bevacizumab)	For the treatment of breast cancer, colorectal cancer, NSCLC and glioblastoma	For the first-line treatment of RCC (in combination with interferon alfa-2a)	Binds to and inhibits the biologic activity of human VEGF/Anti-angiogenesis agent	IV infusion	sBLA for RCC filed October 2008. A response to the sBLA is expected August 2009.
Genentech and Biogen Idec/ Rituxan® (rituximab)	For the treatment of NHL For the treatment of moderately to severely active RA in patients who have had an inadequate response to one or more TNF inhibitors	In combination with standard chemotherapy for the treatment of CLL	Reduces the amount of CD20-positive B-cells in the blood/Therapeutic antibody	IV infusion	sBLA filed May 2009.
Genzyme/ Clolar® (clofarabine)	For the treatment of pediatric patients (1 to 21 years old) with relapsed or refractory acute lymphoblastic leukemia after at least two prior regimens	For the treatment of adult patients with AML	Inhibits DNA synthesis/Purine nucleoside metabolic inhibitor	IV infusion	Designated as an orphan drug. sNDA filed November 2008. A response to the sNDA is expected September 2009.
GlaxoSmithKline/ Tykerb® (lapatinib)	In combination with Xeloda® (capecitabine) for the treatment of patients with advanced or metastatic breast cancer whose tumors over express HER2 and who have received prior therapy, including an anthracycline, a taxane and Herceptin® (trastuzumab)	For the first-line treatment of hormone-sensitive, metastatic breast cancer in combination with anti-hormonal therapy	Reduces tumor cell growth and blood supply/Tyrosine kinase inhibitor	Oral	sNDA filed April 2009. A response to the sNDA is expected February 2010.
Novartis/ Tasigna® (nilotinib)	For the treatment of chronic and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia	For the treatment of gastrointestinal stromal tumor (GIST) in patients who have failed both Gleevec® (imatinib) and Sutent® (sunitinib) therapies	Inhibits Bcr-Abl kinase/Tyrosine kinase inhibitor	Oral	sNDA filing anticipated in 2009.
OSI Pharmaceuticals and Genentech/ Tarceva® (erlotinib)	For the treatment of advanced NSCLC after failure of at least one prior chemotherapy regimen For the first-line treatment of advanced pancreatic cancer in combination with Gemzar® (gemcitabine)	First-line maintenance therapy in patients with advanced NSCLC who have not progressed following first-line treatment with platinum-based chemotherapy	Reduces tumor cell growth and blood supply/Epidermal growth factor receptor (EGFR) inhibitor	Oral	sNDA filed March 2009. A response to the sNDA is expected January 2010.

New Indications in the Pipeline (continued)

Manufacturer/ Drug Name	Current Indication	Investigational Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology					
Pfizer/ Sutent® (sunitinib)	For the treatment of GIST and advanced RCC	For the treatment of colorectal cancer, metastatic breast cancer and NSCLC	Reduces tumor cell growth and blood supply/Multikinase inhibitor	Oral	Phase III trials ongoing.
Spectrum Pharmaceuticals / Zevalin® (ibritumomab tiuxetan)	For the treatment of relapsed or refractory, low- grade or follicular B-cell NHL	As consolidation therapy for patients with follicular B-cell NHL who achieve a response to first-line therapy	Binds to the CD20 antigen on B-cells/ Radioimmuno- therapy	IV injection	sBLA filed October 2008. FDA granted priority review status December 2008. A response to the sBLA is expected July 2009.
Osteoporosis					
Novartis/ Reclast® (zoledronic acid)	For the treatment of Paget's disease and PMO	For the treatment of glucocorticoid-induced osteoporosis (GIO)	Inhibits osteoclast- mediated bone resorption/IV bisphosphonate	IV infusion	sNDA filed 2008.

Glossary of Terms

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 August 11, 2008, the FDA has issued a complete response letter to the applicant in place of an approvable letter.

BLA – stands for “biologic 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.

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 status – 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 that 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.

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

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.

Risk evaluation and mitigation strategy (REMS)– is 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 biologic 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-naïve HIV – Patients who have never been treated for HIV before.

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*Information in the report is current as of May 2009, and was accessed on May 19, 2009.

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