



Specialty Pharmacy Pipeline Report

Third 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.

Omacetaxine

ChemGenex Pharmaceuticals has developed omacetaxine for the treatment of chronic myeloid leukemia (CML) in patients who have failed Gleevec® (imatinib) and have the T315I Bcr-Abl point mutation. CML is a type of cancer that causes the body to produce a significant number of white blood cells, which, depending on the phase of the condition, may interfere with the proper functioning of normal blood cells. Treatment of CML with Gleevec has shown to be very successful; however, some patients treated with Gleevec become resistant or intolerant to therapy over time. Sprycel® (dasatinib) and Tasigna® (nilotinib) are both approved to treat CML in patients who fail Gleevec therapy since these medications can inhibit most of the Bcr-Abl mutations that cause Gleevec resistance, with the exception of the T315I mutation.

Omacetaxine is a first-in-class cetaxine that inhibits protein translation of oncoproteins. In an open label phase II/III study, the use of omacetaxine administered subcutaneously (SC) in CML patients who had failed Gleevec and who had the highly drug resistant T315I mutation was investigated. Data from 66 patients was collected, including 40 patients with chronic phase CML, 16 with accelerated phase CML and 10 with

blast phase CML. The primary endpoint of the trial was complete hematologic response (CHR) rates. In chronic phase patients, the CHR rate was 85 percent with a median response duration of 8.9 months; in accelerated phase patients, the CHR rate was 31 percent with a median response duration of 4.1 months; and in blast phase patients, the CHR rate was 20 percent with a median response duration of 3.3 months. ChemGenex initiated a rolling submission of a New Drug Application (NDA) for omacetaxine on July 1, 2008. The company plans to complete the NDA submission by the end of 2009.

Velaglucerase alfa

Gaucher disease is the most common lysosomal storage disorder. In the United States, the estimated occurrence is approximately one in 40,000 births, and among those of Ashkenazi Jewish descent, it is one in 400 to 800 births. Gaucher disease is the result of a defect in the lysosomal enzyme glucocerebrosidase. This defect causes the build up of glucocerebroside in the body's cells, resulting in a broad range of signs and symptoms including abnormal blood counts, enlarged liver or spleen, destructive bone disease and sometimes lung involvement. Of the three main types of Gaucher disease, the majority of Gaucher patients have Type 1

Gaucher disease. Cerezyme[®] (imiglucerase), an enzyme replacement therapy, and Zavesca[®] (miglustat), a substrate reduction therapy, are currently approved for Type 1 Gaucher disease.

Shire has developed a new enzyme replacement therapy, velaglucerase alfa, for the treatment of Type 1 Gaucher disease. This product is produced in a continuous human cell line using a proprietary gene-activation technology and has an identical amino acid sequence to the naturally occurring glucocerebrosidase. Velaglucerase alfa is administered by an intravenous (IV) infusion every two weeks. The FDA recently accepted Shire's treatment protocol for velaglucerase, which allows physicians to treat patients with velaglucerase alfa prior to FDA approval and commercial launch of the product. Shire initiated a rolling submission of an NDA for velaglucerase alfa on July 30, 2009. The company plans to complete the NDA submission by the end of this year.

Benlysta[™] (belimumab)

Human Genome Sciences and GlaxoSmithKline are developing Benlysta[™] for the treatment of systemic lupus erythematosus (SLE). SLE is a multisystem, autoimmune, connective-tissue disorder that predominately affects females with a prevalence of 40 to 200 cases per 100,000 persons. Since SLE can affect multiple organs, patients may experience a wide range of signs and symptoms including skin rashes, mouth lesions, inflammation of the kidney, mood disorders, headaches, heart complications and blood abnormalities. The treatment of SLE can vary, depending on the presentation of the disease.

Benlysta inhibits the activity of the B-lymphocyte stimulator (BLyS). BLyS is a naturally occurring protein discovered by Human Genome Sciences that is required for the development of B-lymphocyte cells into mature plasma B cells, which in turn produce antibodies.

The phase III program for Benlysta includes two double-blind, placebo-controlled trials to evaluate the efficacy and safety of two different doses of Benlysta plus standard of care versus placebo plus standard of care in patients with SLE. Benlysta is administered as an IV infusion. The design of the two trials is similar except for the study duration; BLISS-52 is a 52-week study while BLISS-76 is a 76-week study. The primary endpoint of the trials was patient response rate as measured by disease activity scores. The results from BLISS-52 demonstrated patient response rates of 57.6 percent for the Benlysta 10 mg/kg group, 51.7 percent for the Benlysta 1 mg/kg group and 43.6 percent for the placebo group. Data from BLISS-76 is expected in November 2009. If the results from the second trial are positive, Human Genome Sciences and GlaxoSmithKline plan to file a biologic license application (BLA) in the first half of 2010.

Medications Recently Approved

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Approval Date	Comments
Human Immunodeficiency Virus (HIV)					
Merck/ Isentress® (raltegravir)	For the treatment of adult patients starting HIV therapy for the first time (treatment-naïve)	Inhibits the insertion of the HIV viral DNA into human DNA/ Integrase inhibitor	Oral	07/31/2009	Previously approved for treatment-experienced adult patients.
Inflammatory Diseases					
Novartis/ Ilaris® (canakinumab)	For the treatment of cryopyrin-associated periodic syndromes in adults and children 4 years of age and older, including familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS)	Targets interleukin (IL)-1β/ IL-1β inhibitor	SC injection	06/17/2009	First approved treatment for patients as young as 4 years old with a diagnosis of FCAS or MWS.
Oncology					
Genentech/ Avastin® (bevacizumab)	For the treatment of metastatic renal cell carcinoma (RCC) in combination with interferon alfa	Binds to and inhibits the biologic activity of human vascular endothelial growth factor/Anti-angiogenesis agent	IV infusion	07/31/2009	Previously approved for the treatment of colorectal cancer, non-small cell lung cancer (NSCLC), breast cancer and glioblastoma
Osteoporosis					
Eli Lilly/ Forteo® (teriparatide)	For the treatment of glucocorticoid-induced osteoporosis (GIO)	Stimulates bone formation/ Parathyroid hormone analogue	SC injection	07/22/2009	Previously approved for the treatment of men and postmenopausal women with osteoporosis who are at high risk for fracture
Novartis/ Reclast® (zoledronic acid)	For the treatment and prevention of GIO	Inhibits osteoclast-mediated bone resorption/IV bisphosphonate	IV infusion	03/13/2009	Previously approved for the treatment and prevention of osteoporosis in postmenopausal women and the treatment of osteoporosis in men
Pulmonary Arterial Hypertension					
Actelion/ Tracleer® (bosentan)	For the treatment of pulmonary arterial hypertension (PAH) in patients with WHO (World Health Organization) Class II symptoms, to improve exercise ability and decrease the rate of clinical worsening	Reduces vascular smooth muscle constriction/ Endothelin receptor antagonist	Oral	08/07/2009	Previously approved for Class III-IV symptoms
United Therapeutics and Lung Rx/ Tyvaso (treprostinil)	To increase walk distance in patients with PAH WHO Class III symptoms	Dilates pulmonary blood vessels/ Prostacyclin analogue	Inhalation	07/30/2009	Also available as a SC or IV infusion under the trade name Remodulin®

Pipeline Medications in Phase III Trials

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Alpha-1 Antitrypsin Deficiency				
Kamada/ Alpha-1 antitrypsin (AAT)	For the treatment of AAT deficiency	Replacement therapy/ Human plasma derived AAT	IV infusion	BLA filed June 2009. A response to the BLA is expected April 2010.
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 Disorders				
GlaxoSmithKline/ Bosatria® (mepolizumab)	For the treatment of hypereosinophilic syndrome	Binds to and inactivates 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 a special protocol assessment (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	Designated as an orphan drug with fast track status. Rolling NDA initiated July 2009. Available through an expanded access program.
Hepatitis				
Human Genome Sciences and Novartis/ Albupheron® (albinterferon alfa-2b)	In combination with ribavirin for the treatment of hepatitis C virus (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	Phase III data expected in 2010.
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. FDA accepted resubmission of BLA. A response to the BLA is expected December 2009.
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. The trials are scheduled to be completed this year.
Theratechnologies/ Tesamorelin	For the treatment of HIV-associated lipodystrophy	Reduces visceral adipose tissue/Growth hormone-releasing factor analogue	SC injection	NDA filed June 2009. A response to the NDA is expected April 2010.

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. BLA amended. A response to the BLA is expected August 2009.
Genentech, Roche and Biogen/ Ocrelizumab	For the treatment of rheumatoid arthritis (RA) and lupus nephritis	Binds to B-cells and leads to cell death/Second generation anti-CD20	IV injection	BLA filing planned for 2010.
Human Genome Sciences and GlaxoSmithKline/ Benlysta™ (belimumab)	For the treatment of SLE	Inhibits the activity of BLYS/BLYS-specific inhibitor	IV infusion	BLA filing planned for the first half of 2010.
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. FDA accepted the resubmission of the BLA. A response to the BLA is expected January 2010.
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. Complete response letter August 2009. The FDA has requested additional information including a proposal for a risk evaluation and mitigation strategy. Savient plans to resubmit its BLA in early 2010.
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	FDA granted fast track status. Primary endpoint was not met in phase III trial and ongoing clinical trials discontinued.

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/ Immunomodulatory agent	Oral	NDA filing planned for end of 2009.
Sanofi-aventis/ Teriflunomide	For the treatment of relapsing forms of MS	Inhibits pyrimidine synthesis/ Immunomodulatory 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. FDA granted fast track status.
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				
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. FDA granted priority review status May 2009. A response to the NDA is expected September 2009.
AstraZeneca/ Zactima® (vandetanib)	For the second-line treatment of NSCLC	Reduces tumor cell growth and blood supply/Multikinase inhibitor	Oral	NDA filed July 2009. A response to the NDA is expected May 2010.
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.
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 with current anthracyclines. Rolling NDA submission completed June 2009.
Centocor 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/Nonplatinum antitumor agent	IV infusion	NDA filed November 2008. A response to the NDA is expected September 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. Primary endpoint was not met in phase III trial June 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
ChemGenex Pharmaceuticals/ Omacetaxine	For the treatment of CML in patients who failed Gleevec (imatinib) and have the T315I Bcr-Abl point mutation	Inhibits protein translation of oncoproteins/Cetaxine	SC injection	Rolling NDA submission initiated July 2008. Completed application expected in the second half of 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 the fourth quarter 2009.
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 was expected July 2009; however, additional data was submitted and the review period was extended by three months. A response to the BLA is now expected October 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. Data from a phase III trial are expected in the fourth quarter of 2009.
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/mammalian target of rapamycin	Oral	NDA filing planned for 2010.
Poniard Pharmaceuticals/ Picoplatin	For the second-line treatment of small cell lung cancer (SCLC)	Interferes with cell division and genetic transcription processes, leading to cell death/Platinum agent	IV infusion	Designed to overcome platinum resistance. Rolling NDA submission planned for the end of 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
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/ Prolia™ (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.
Pulmonary Arterial Hypertension				
Pfizer/ Theelin™ (sitaxsentan)	For the treatment of 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 studies ongoing.
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 the fourth quarter of 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	Intramuscular (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.
Transplantation				
Osiris Therapeutics/ Prochymal	For the treatment of acute graft versus host disease	Repairs damaged tissue/Stem cell product	IV infusion	Designated as an orphan drug with fast track status. Rolling BLA initiated April 2009.

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— Sandostatin LAR®. NDA filing planned for 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. The FDA requested an additional clinical study. Gilead has two ongoing studies evaluating the product. Available through an expanded access program.
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 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. Complete response letter July 2009. The FDA has requested additional information.

*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/ Anti-immunoglobulin E agent	SC injection	Supplemental biologic license application (sBLA) filed December 2008. A response to the sBLA is expected October 2009.
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. Complete response letter June 2009. The FDA requested an additional clinical study.
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	Supplemental new drug application (sNDA) filed June 2006. Not approvable letter May 2007. sNDA resubmitted with filing 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 antirheumatic 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 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 overexpress 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 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, breast cancer, NSCLC, hepatocellular cancer, HRPC and pancreatic cancer	Reduces tumor cell growth and blood supply/Multikinase inhibitor	Oral	Phase III trial in colorectal cancer discontinued June 2009.
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. Complete response letter July 2009. FDA accepted resubmission of sBLA. A response to the sBLA is expected September 2009.

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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Manufacturers' web sites

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www.biopharminsight.com

ClinicalTrials.gov
www.clinicaltrials.gov

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*Information in the report is current as of August 2009, and was accessed on August 14, 2009.

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