



Specialty Pharmacy Pipeline Report

First 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.

Pegloticase

Savient Pharmaceuticals has filed a biologic license application (BLA) for pegloticase for the treatment of gout in patients for whom conventional treatment is contraindicated or ineffective. Gout is the most common type of inflammatory arthritis and is caused by elevated levels of uric acid. The Third National Health and Nutrition Examination Survey estimated the prevalence of gout in the U.S. population between 1988 and 1994 to be 5.1 million.

There are two parts to gout management: treatment of acute gout attacks and chronic management of elevated uric acid levels to prevent attacks. Acute attacks may be managed with anti-inflammatory agents such as nonsteroidal anti-inflammatory drugs, colchicine or corticosteroids. Chronic therapy with allopurinol or probenecid may be used to reduce uric acid levels.

Savient Pharmaceuticals estimates there are between 25,000 and 100,000 treatment-failure patients in the United States.

Pegloticase is an intravenous (IV) infusion that has been shown to lower the plasma level of uric acid. In two phase III clinical trials in patients with treatment-failure gout, pegloticase 8 mg administered by a two-hour infusion every two weeks or every four weeks was compared to placebo. The primary endpoint of these studies was the normalization of plasma uric acid during months three and six of the trials. In the intent-to-treat analysis, the mean responder rates were pooled across both studies. The mean responder rates for the pegloticase every-two-weeks group was 42 percent, the pegloticase every-four-weeks group was 35 percent, and the placebo group was 0 percent. Additional analysis showed a significant reduction in the number of tender and swollen joints in the patients receiving pegloticase. Infusion reactions occurred in 33 percent of the patients receiving pegloticase and typically involved back or chest pain, muscle cramps, sweating and flushing.

Pegloticase is designated as an orphan drug. The BLA was filed in October 2008, and the FDA granted priority review status in December 2008. A response to the BLA is expected in April 2009.

Fampridine-SR, Fingolimod and Mylinax® (oral cladribine)

According to the National Multiple Sclerosis Society, there are approximately 400,000 people in the United States with multiple sclerosis (MS), a chronic condition that affects the central nervous system. Management of

MS involves treatment of acute relapses, prevention of relapses, disease progression and management of symptoms.

Acorda Therapeutics has developed fampridine-SR to improve walking ability in people with MS. Recent surveys indicate that 64 percent of people with MS have a walking disability. Fampridine-SR is an oral selective neuronal potassium channel blocker that improves impulse conduction in nerve fibers with damaged myelin.

In one phase III study, fampridine-SR 10 mg twice daily was compared to placebo. The primary endpoint of the trial was response on the timed 25-foot walk. A responder was defined as a patient whose walking speed was faster at a majority of the four on-treatment visits than any speed measured during the five off-treatment visits. In this trial, a significantly greater proportion of patients taking fampridine-SR were responders compared with patients taking placebo (42.9 percent and 9.3 percent respectively). The most common adverse events reported in the fampridine-SR group were urinary tract infection, insomnia, headache, dizziness and nausea. Fampridine-SR is designated as an orphan drug. A new drug application (NDA) was filed in January 2009, with a response expected by November 2009.

Fingolimod, an oral immunomodulatory agent in development by Novartis, is an investigational medication for the treatment of relapsing-remitting MS. Fingolimod is thought to work by reducing inflammation and myelin damage in the brain and spinal cord. Currently, none of the disease-modifying treatments approved for MS are available in an oral formulation.

In a phase III trial, fingolimod 0.5 mg or 1.25 mg once daily was compared to a once weekly intramuscular (IM) injection of Avonex[®] (interferon beta-1a). The primary endpoint of the study was annualized relapse rate. Patients in the fingolimod 0.5 mg group experienced a relapse rate of 0.16 compared with a relapse rate of 0.2 in the fingolimod 1.25 mg group and 0.33 in the Avonex group. The reductions in relapses were significant for both the fingolimod 0.5 mg group (52 percent reduction) and the fingolimod 1.25 mg group (38 percent reduction) compared with the Avonex group. The most common adverse events reported in all three groups were headache,

nasopharyngitis and fatigue. Influenza-like symptoms were reported in 37 percent of Avonex patients and 4 percent of fingolimod patients. An NDA filing for fingolimod is planned for the end of 2009.

Merck Serono has developed an oral formulation of cladribine, Mylinax[®], for the treatment of relapsing forms of MS. An injectable formulation of cladribine, Leustatin[®], is currently available for the treatment of hairy cell leukemia, and is administered by IV infusion. Mylinax is thought to be effective in MS because it interferes with lymphocytes that are involved in the pathology of MS.

The efficacy of Mylinax in reducing relapses was evaluated in a two-year, randomized, double-blind, placebo-controlled trial. Patients were assigned to one of three groups: low-dose Mylinax, high-dose Mylinax or placebo. The primary endpoint of the trial was annualized relapse rate. Patients in the low-dose Mylinax group experienced a relapse rate of 0.14 compared with a relapse rate of 0.15 in the high-dose Mylinax group and 0.33 in the placebo group. The reductions in relapses were significant for both the low-dose Mylinax group (58 percent reduction) and the high-dose Mylinax group (55 percent reduction) compared to placebo. Lymphopenia (low lymphocyte levels) occurred more frequently in the Mylinax groups. The frequencies of other adverse events were comparable between the Mylinax and placebo groups. Mylinax is designated as an orphan drug with fast track status. Merck Serono is planning to file an NDA for Mylinax in mid-2009.

Arzerra[™] (ofatumumab)

Genmab and GlaxoSmithKline have submitted a BLA for Arzerra[™] to treat patients whose chronic lymphocytic leukemia (CLL) is refractory to previous therapies. CLL is the most common form of leukemia in adults in the Western world, accounting for nearly 25 percent of all leukemias.

Arzerra is a monoclonal antibody that targets a specific antibody binding site of CD20 on B-cells. The efficacy of Arzerra is being evaluated in a phase III study of patients with CLL refractory to both Fludara[®] (fludarabine) and Campath[®] (alemtuzumab) and in patients refractory to Fludara who are inappropriate candidates for Campath. In the study, patients receive eight weekly IV infusions of Arzerra, followed by four monthly infusions. The primary endpoint of the study

is assessment of objective response. At a preplanned interim analysis, the reported overall objective response rate was 58 percent in the patients refractory to both Fludara and Campath and 47 percent in the patients refractory to Fludara and ineligible for

Campath. The most common adverse events reported were infusion reactions and infections.

A BLA for Arzerra was filed in January 2009, with a response expected in November 2009.

Medications Recently Approved

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Approval Date	Comments
Blood Disorder					
CSL Behring/ RiaSTAP™ (fibrinogen concentrate [human])	For the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia	Replaces deficient fibrinogen/Factor I	IV injection	01/16/09	First approved treatment for this indication.
GTC Therapeutics and Ovation Pharmaceuticals/ ATryn® (antithrombin [recombinant])	For the prevention of thromboembolic events in patients with hereditary antithrombin deficiency who are undergoing high-risk surgical and childbirth procedures	Replaces antithrombin/ Recombinant human antithrombin	IV injection	02/06/09	First approved biological product produced by genetically engineered animals.
Immune Thrombocytopenic Purpura					
GlaxoSmithKline/ Promacta® (eltrombopag)	For the treatment of thrombocytopenia in patients with chronic immune thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy	Stimulates the proliferation and differentiation of megakaryocytes (bone marrow cells that give rise to platelets)/ Thrombopoietin receptor agonist	Oral	11/20/08	First oral thrombopoietin receptor agonist approved for adult patients with chronic ITP. Walgreens Specialty Pharmacy is a preferred distributor, a distinction given to a select number of specialty pharmacies based on criteria established by the pharmaceutical company.
Oncology					
Antisoma/ Oral fludarabine	For the treatment of adult patients with relapsed or refractory B-cell CLL after at least one standard alkylating-agent containing regimen	Inhibits DNA and RNA synthesis/ Purine nucleotide antimetabolite agent	Oral	12/18/08	Antisoma plans to make the product available to U.S. patients through a commercialization deal, which is expected to conclude in early 2009.
Cephalon/ Treanda® (bendamustine)	For the treatment of indolent B-cell non-Hodgkin's lymphoma (NHL) that has progressed during or within six months of treatment with Rituxan® (rituximab) or a Rituxan-containing regimen	Causes cell death and disrupts cell division/Hybrid alkylating agent	IV infusion	10/31/08	Previously approved for the treatment of CLL.

Medications Recently Approved (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Approval Date	Comments
Oncology					
Ferring Pharmaceuticals/ Degarelix	For the treatment of advanced prostate cancer	Suppresses the release of testosterone/ Gonadotropin-releasing hormone (GnRH) receptor antagonist	SC injection	12/24/08	Potential trade names are still under review with the FDA.
Transplant					
Genzyme/ Mozobil™ (plerixafor)	In combination with granulocyte-colony stimulating factor to mobilize hematopoietic stem cells for collection and autologous transplantation in patients with NHL and multiple myeloma	Inhibits binding of stromal-derived factor 1 to chemokine receptor 4/ Chemokine receptor antagonist	SC injection	12/15/08	Has the potential to decrease the number of apheresis days required to collect a sufficient number of cells for transplant and may also reduce the number of patients who require a second mobilization procedure due to a failure to collect sufficient numbers of cells for transplant.

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™ (eprodissate), 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/ 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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Cystic Fibrosis				
Inspire Pharmaceuticals/ Denufosol	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/ Velaglucerase 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/ Albupheron® (albinterferon alfa-2b)	In combination with ribavirin for the treatment of chronic hepatitis C virus (HCV) infection	Inhibits viral replication/Interferon	Injection	Phase III data expected by spring 2009 and 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	Prevents virus replication/Protease inhibitor	Oral	Enrollment completed for phase III registration studies January 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.
Dyax/ DX-88 (ecallantide)	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. A response to the BLA is expected March 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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
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.
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 and Schering-Plough/ 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	BLA filed June 2008. A response to the BLA is expected April 2009.
Centocor/ 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 Risk Evaluation and Mitigation Strategy (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.
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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Inflammatory Diseases				
Savient Pharmaceuticals/ 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 is expected April 2009.
Multiple Sclerosis				
Acorda Therapeutics/ Fampridine-SR	To improve walking ability in patients with MS	Improves impulse conduction in nerve fibers with damaged myelin/Selective neuronal potassium channel blocker	Oral	Designated as an orphan drug. NDA filed January 2009. A response to the NDA is expected November 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.
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.
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 non-small cell lung cancer (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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
Cell Therapeutics/ Pixantrone	For the treatment of relapsed aggressive 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 planned for first quarter 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. The FDA will accept either a positive interim or final analysis of survival from the ongoing phase III trial to amend the BLA. The final analysis is expected mid-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.
Genmab and GlaxoSmithKline/ Arzerra™ (ofatumumab)	For the treatment of refractory CLL	Targets the binding site of CD20 on B-cells/Anti-CD20 monoclonal antibody	IV infusion	BLA filed January 2009. A response to the BLA is expected November 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. Genta has filed an appeal of this decision.
Lorus Therapeutics and Zor Pharmaceuticals/ Virulizin®	For first-line treatment of advanced pancreatic cancer in combination with Gemzar® (gemcitabine)	Increases the cytogenic effects of macrophages/Biologic response modifier	Intramuscular (IM) injection	Rolling NDA accepted July 2005. Designated as an orphan drug with fast track status.
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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
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 (mTOR) inhibitor	Oral	NDA filing planned for 2010.
Novartis/ Afinitor (everolimus, RAD001)	For the treatment of advanced renal cell carcinoma (RCC) and neuroendocrine tumors	Inhibits tumor cell growth and the formation of new blood vessels/mTOR inhibitor	Oral	NDA for RCC filed July 2008. FDA granted priority review status September 2008. A response to the NDA is expected March 2009.
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 fourth quarter 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.
Pulmonary Arterial Hypertension				
Pfizer/ Thelin [™] (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.
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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Transplant				
Novartis/ Certican™ (everolimus)	For the prevention of solid organ transplant rejection in combination with Neoral® (cyclosporine)	Inhibits proliferation of T-cells, the cells involved in the rejection process/ Immunosuppressant (mTOR inhibitor)	Oral	NDA filed December 2002. First approvable letter October 2003. Second approvable letter August 2004. FDA Advisory Committee recommended that additional study data be provided to support the NDA November 2005. Clinical trials are ongoing.

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. The FDA notified Gilead that an additional study will be required; however, Gilead is working with the FDA to determine whether further analyses of the existing data could lead to approval. 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.

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
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	This formulation of Trelstar is 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/ Viveta (treprostinil)	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. A response to the NDA is expected April 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.
Hereditary Angioedema					
Lev Pharmaceuticals/ 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.

New Indications in the Pipeline (continued)

Manufacturer/ Drug Name	Current Indication	Investigational Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
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 antiretroviral 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.
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
Inflammatory Diseases					
UCB/ Cimzia® (certolizumab pegol)	For the treatment of Crohn's disease	For the treatment of moderate to severe or active RA	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	BLA filed December 2007. Complete response letter January 2009. The FDA has requested a new safety update with all clinical data.
Oncology					
Cell Therapeutics/ Zevalin® (ibritumomab tiuxetan)	For 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 April 2009.
Genentech/ Avastin® (bevacizumab)	For the treatment of breast cancer, colorectal cancer and NSCLC	For the first-line treatment of RCC (in combination with interferon alfa-2a) and for the treatment of relapsed glioblastoma multiforme	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. sBLA for glioblastoma filed November 2008. A response to the sBLA is expected 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.
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.

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.
Osteoporosis					
Eli Lilly/ Forteo® (teriparatide)	For the treatment of men and postmenopausal women with osteoporosis who are at high risk for fracture	For the treatment of glucocorticoid-induced osteoporosis (GIO)	Stimulates bone formation/ Parathyroid hormone analogue	SC injection	sNDA filed February 2007. Eli Lilly reported receiving an approvable letter April 2008.
Novartis/ Reclast® (zoledronic acid)	For the treatment of Paget's disease and PMO	For the treatment of 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 – 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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www.biopharminsight.com

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*Information in the report is current as of February 2009, and was accessed on February 6, 2009.

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