

Specialty Pharmacy Pipeline Report

Fourth 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.

Votrient™ (pazopanib)

On October 19, 2009, the FDA approved GlaxoSmithKline's *Votrient™* for the treatment of patients with advanced renal cell carcinoma (RCC). According to the American Cancer Society, there will be more than 57,700 new cases of kidney cancer and approximately 13,000 deaths from the disease in 2009.

Votrient is an orally administered multikinase inhibitor that prevents the growth and spread of cancer by slowing tumor growth and reducing the tumor's blood supply. Other orally administered treatments for RCC include *Sutent®* (sunitinib) and *Nexavar®* (sorafenib), also multikinase inhibitors, as well as *Afinitor®* (everolimus), a mammalian target of rapamycin (mTOR) inhibitor.

In a phase III trial, *Votrient* (800 mg once daily) was compared to placebo in 233 treatment-naïve and 202 cytokine-pretreated patients with RCC. The primary endpoint of the trial was progression-free survival (PFS). In the overall study population, the median PFS was 9.2 months with *Votrient* and 4.2 months with placebo. The median PFS for treatment-naïve patients was 11.1 months with *Votrient* and 2.8 months with placebo, while the

cytokine-pretreated patients experienced a median PFS of 7.4 months with *Votrient* and 4.2 months with placebo. The most common side effects of *Votrient* include diarrhea, hypertension, hair color changes, nausea, anorexia and vomiting.

Replagal® (agalsidase alfa)

Shire has developed *Replagal®* for the treatment of Fabry disease, a lysosomal storage disorder caused by a deficiency in alpha-galactosidase A. This enzyme deficiency leads to a build up of globotriaosylceramide in the body's cells, ultimately leading to organ damage. Fabry disease is an X-linked disorder, predominately affecting males with an incidence of approximately 1:40,000 to 1:60,000. Affected females are usually carriers and may have disease symptoms but rarely have full-blown classic Fabry disease.

Fabrazyme® (agalsidase beta) is the only enzyme replacement therapy approved by the FDA to treat Fabry disease. *Fabrazyme* is a recombinant human alpha-galactosidase A enzyme, which is derived from a mammalian cell line. *Replagal* is also a recombinant human alpha-galactosidase A enzyme but is derived from a human cell line. *Replagal* is administered as an intravenous (IV) infusion every two weeks.

The FDA recently approved Shire's treatment protocol for Replagal, which allows physicians to treat patients with Replagal prior to FDA approval and commercial launch of the product. Shire plans to file a biologic license application (BLA) for Replagal by the end of 2009.

Tafamidis

Tafamidis is an investigational agent for the treatment of transthyretin (TTR) amyloid polyneuropathy. This rare, hereditary disease is characterized by the deposition of amyloid fibrils (abnormal proteins) in various tissues, predominately in the peripheral and autonomic nervous systems, as well as the heart. In the United States, an estimated 6,400 individuals are thought to be affected by TTR amyloid polyneuropathy.

Tafamidis is a TTR stabilizer that inhibits the formation of TTR amyloid fibrils. In a phase II/III trial, tafamidis, 20 mg by mouth once daily, was compared to placebo in 128 patients. The primary endpoints of the trial were disease progression and quality of life. After 18 months, no disease progression was observed in 60 percent of the tafamidis patients and in 38 percent of the placebo patients. A significant deterioration in quality of life was also observed in the placebo patients, compared with the tafamidis patients.

The FDA has designated tafamidis as an orphan drug with fast track status. FoldRx Pharmaceuticals plans to file a new drug application (NDA) for tafamidis in 2010.

Medications Recently Approved

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Approval Date | Comments |
|--|--|--|-----------------------------|------------------|--|
| Hereditary Angioedema (HAE) | | | | | |
| CSL Behring/ Berinert® P (C1 inhibitor) | For the treatment of acute abdominal or facial attacks of HAE | Replaces deficient C1 esterase inhibitor/C1 esterase inhibitor replacement therapy | IV infusion | 10/09/2009 | First treatment approved for this indication. |
| Inflammatory Diseases | | | | | |
| Bristol-Myers Squibb/ Orencia® (abatacept) | For the treatment of patients with moderate to severe rheumatoid arthritis (RA) of less than or equal to two years duration | Inhibits T-cell activation/Selective costimulation modulator | IV infusion | 8/25/2009 | Orencia is also approved for the treatment of polyarticular juvenile idiopathic arthritis. |
| Centocor/ Stelara™ (ustekinumab) | For the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy | Targets interleukin-12 (IL-12) and interleukin-23 (IL-23)/ Dual IL inhibitor | Subcutaneous (SC) injection | 9/25/2009 | First product approved in a new class of biologics. |
| Multiple Sclerosis (MS) | | | | | |
| Novartis/ Extavia® (interferon beta-1b) | For the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations | Mechanism of action in MS is unknown/ Interferon | SC injection | 8/14/2009 | Contains the same active ingredient as Betaseron®. |
| Oncology | | | | | |
| Allos Therapeutics/ Foloty™ (pralatrexate) | For the treatment of patients with relapsed or refractory peripheral T-cell lymphoma | Interferes with DNA synthesis and triggers cancer cell death/ Antifolate | IV injection | 9/24/2009 | First treatment approved for this indication. |

Medications Recently Approved (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Approval Date | Comments |
|---|---|---|----------------------------|------------------|--|
| Oncology | | | | | |
| Genmab and GlaxoSmithKline/ Arzerra™ (ofatumumab) | For the treatment of patients with chronic lymphocytic leukemia (CLL) refractory to fludarabine and Campath® (alemtuzumab) | Targets the binding site of CD20 on B-cells/Anti-CD20 monoclonal antibody | IV infusion | 10/26/2009 | Approved under the FDA's accelerated approval mechanism. |
| GlaxoSmithKline/ Votrient™ (pazopanib) | For the treatment of patients with RCC | Reduces tumor cell growth and blood supply/Tyrosine kinase inhibitor | Oral | 10/19/2009 | 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. |
| Gloucester Pharmaceuticals/ Romidepsin | For the treatment of cutaneous T-cell lymphoma in patients who have received at least one prior systemic therapy | Inhibits tumor cell growth, causes cell death and inhibits the formation of new blood vessels/Histone deacetylase inhibitor | IV infusion | 11/05/2009 | First product approved in a new class of cancer medications. |
| Spectrum Pharmaceuticals/ Zevalin® (ibritumomab tiuxetan) | For the treatment of patients with previously untreated follicular non-Hodgkin's lymphoma (NHL) who achieve a partial or complete response to first-line chemotherapy | Binds to the CD20 antigen on B-cells/ Radioimmunotherapy | IV injection | 9/03/2009 | Previously approved for the treatment of relapsed or refractory, low-grade or follicular NHL. |

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. |
| Amyloidosis | | | | |
| FoldRx Pharmaceuticals/ Tafamidis | For the treatment of TTR amyloid polyneuropathy | Inhibits TTR amyloid fibril formation/TTR stabilizer | Oral | Designated as an orphan drug with fast track status. NDA filing expected in 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. Phase III results expected the second quarter 2010. NDA filing planned for 2010. |

Pipeline Medications in Phase III Trials (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|--|--|---|----------------------------|--|
| Cystic Fibrosis (CF) | | | | |
| Inspire Pharmaceuticals/ Denufosol | For the treatment of CF | Designed to enhance mucosal hydration and mucociliary clearance/ Second generation P2Y ₂ agonist | Inhalation | Designated as an orphan drug with fast track status. Primary endpoint achieved in first phase III trial June 2008. Enrollment completed in second phase III study November 2009. |
| Enzyme Replacement Therapy | | | | |
| Protalix/ Uplyso (taliglucerase alfa), formerly prGCD | For the treatment of Gaucher disease | Replaces deficient glucocerebrosidase/ Enzyme replacement therapy | IV infusion | Primary endpoint achieved in phase III trial October 2009. NDA filing anticipated fourth quarter 2009. |
| Shire/ Replagal® (agalsidase alfa) | For the treatment of Fabry disease | Replaces deficient alpha-galactosidase A/ Enzyme replacement therapy | IV infusion | Designated as an orphan drug. BLA filing expected fourth quarter 2009. Available through an expanded access program. |
| Shire/ Velaglucerase 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 completed September 2009. FDA granted priority review status November 2009. A response to the NDA is expected February 2010. Available through an expanded access program. |
| Hepatitis | | | | |
| Human Genome Sciences and Novartis/ Zalbin™ (albinterferon alfa-2b), formerly Albuferon® | In combination with ribavirin for the treatment of hepatitis C virus (HCV) infection | Inhibits viral replication/Interferon | SC injection | Primary endpoint achieved in two pivotal phase III trials April 2009. BLA filing anticipated by end of 2009. |
| Merck/ Boceprevir | In combination with PegIntron® (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 | Phase III studies expected to be completed mid-2010. |
| 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. NDA filing anticipated in the second half of 2010. |

Pipeline Medications in Phase III Trials (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|--|--|--|------------------------------------|--|
| Hereditary Angioedema (HAE) | | | | |
| 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. 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) | | | | |
| Merck/ 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 (CCR5) | Oral | Patient enrollment for two phase III trials completed during 2009. |
| 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. |
| Infertility | | | | |
| Merck/ Corifollitropin alfa | For the development of multiple follicles and pregnancy in women participating in an assisted reproductive technology program | Stimulates ovarian follicular growth/ Sustained follicle stimulant | SC injection | Primary endpoints achieved in phase III trial July 2009. |
| Inflammatory Diseases | | | | |
| Genentech, Roche and Biogen/ Ocrelizumab | For the treatment of 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 systemic lupus erythematosus | Inhibits the activity of B-lymphocyte stimulator (BLyS)/BLyS-specific inhibitor | IV infusion | BLA filing planned for the first half of 2010. |

Pipeline Medications in Phase III Trials (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|--|---|--|----------------------------|---|
| Inflammatory Diseases | | | | |
| 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. 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 (MS) | | | | |
| Acorda Therapeutics/ Amaya (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 originally filed January 2009, then resubmitted April 2009. FDA granted priority review status May 2009. A response to the NDA was expected October 2009; however, additional information was submitted and the review period was extended by three months. A response to the NDA is now expected January 2010. |
| Novartis/ Fingolimod (FTY720) | For the treatment of relapsing-remitting MS | Reduces inflammation and myelin damage in the brain and spinal cord/ Immunomodulatory agent | Oral | Primary endpoint achieved in phase III trial September 2009. 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 | FDA granted fast track status. Two phase III studies have completed enrollment and are currently ongoing. |
| 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 filed July 2009. NDA withdrawn in October 2009 based on an updated analysis that demonstrated no overall survival advantage when Zactima was added to chemotherapy. |

Pipeline Medications in Phase III Trials (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|--|---|---|----------------------------|--|
| Oncology | | | | |
| 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. FDA granted fast track status. Cell Therapeutics to focus on ovarian cancer indication September 2009. |
| Cell Therapeutics/ Pixantrone | For the treatment of relapsed or refractory 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 with current anthracyclines. Rolling NDA submission completed June 2009. A response to the NDA is expected April 2010. |
| 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. Complete response letter September 2009. The FDA has requested additional information. |
| ChemGenex Pharmaceuticals/ Omapro™ (omacetaxine) | For the treatment of chronic myeloid leukemia in patients who failed Gleevec® (imatinib) and have the T315I Bcr-Abl point mutation | Inhibits protein translation of oncoproteins/Cetaxine | SC injection | Designated as an orphan drug with fast track status. Rolling NDA completed September 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. Amended BLA filed November 2009. |
| EpiCept/ Ceplene® (histamine dihydrochloride) | In conjunction with IL-2 as a remission maintenance treatment of acute myeloid leukemia (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. |
| Genta/ Genasense® (oblimersen) | For the treatment of melanoma and relapsed or refractory CLL in combination with chemotherapy and melanoma | Inhibits the production of Bcl-2/Antisense therapy | IV infusion | Designated as an orphan drug. NDA for CLL filed December 2005. Non-approvable letter December 2006. NDA amended June 2008. Complete response letter December 2008. According to preliminary results, one co-primary endpoint not achieved in phase III melanoma trial October 2009. The second co-primary endpoint is too early to evaluate. |

Pipeline Medications in Phase III Trials (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|---|--|---|----------------------------|---|
| Oncology | | | | |
| 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 special protocol assessment (SPA) approval from the FDA for phase III trial in ovarian cancer. FDA granted fast track status. |
| Merck and Ariad Pharmaceuticals/ Ridaforolimus (MK-8669), formerly deforolimus | For the treatment of metastatic sarcoma | Inhibits tumor cell growth and the formation of new blood vessels/mTOR inhibitor | Oral | Designated as an orphan drug with fast track status. NDA filing planned for 2010. |
| Ponard 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. FDA granted fast track status. Rolling NDA submission planned for the end of 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/ 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. Complete response letter October 2009. The FDA has requested additional information. |
| 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 (PAH) | | | | |
| Pfizer/ Thelin™ (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 with fast track status. NDA filed November 2009. |

Pipeline Medications in Phase III Trials (continued)

| Manufacturer/ Drug Name | Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|--|---|--|---------------------------------|---|
| Respiratory Syncytial Virus (RSV) | | | | |
| MedImmune and AstraZeneca/ Numax® (motavizumab) | For the prevention of 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 | | | | |
| Bristol-Myers Squibb/ Belatacept | For the prevention of graft rejection and maintenance of kidney function following renal transplantation | Inhibits T-cell activation/Selective costimulation modulator | IV infusion | BLA filed July 2009. A response to the BLA is expected May 2010. |
| 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. According to preliminary results, primary endpoint not achieved in two phase III trials September 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 | Ambrilia obtained a court order for creditor protection. One phase III trial terminated to help reduce costs. |
| Cystic Fibrosis (CF) | | | | | |
| Gilead Sciences/ Cayston™ (aztreonam lysine) | For the treatment of patients with CF 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. FDA advisory committee to review NDA in December 2009. Available through an expanded access program. |
| Novartis/ TBM100 (tobramycin) | For the treatment of patients with CF 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 (MS) | | | | | |
| Merck Serono and Teva/ 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 filed September 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. |
| Hereditary Angioedema (HAE) | | | | | |
| 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. |
| Human Immunodeficiency Virus (HIV) | | | | | |
| Pfizer/ Selzentry® (maraviroc) | For treatment- experienced patients with CCR5-tropic HIV-1 infection in combination with other antiretroviral therapies | For treatment-naïve patients with CCR5-tropic HIV-1 infection as part of combination therapy | Inhibits entry of virus into human CD4 T-cells/CCR5 antagonist | Oral | Supplemental New Drug Application (sNDA) filed December 2008. FDA advisory committee recommended approval October 2009. |

New Indications in the Pipeline (continued)

| Manufacturer/ Drug Name | Current Indication | Investigational Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|---|---|---|---|----------------------------|---|
| 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 adrenocorticotrop hormone | IM or SC injection | sNDA filed June 2006. Non-approvable letter May 2007. sNDA resubmitted October 2009. |
| Inflammatory Diseases | | | | | |
| 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 tumor necrosis factor (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. Complete response letter October 2009. The FDA does not support the use of Rituxan in this patient population due to the risk of progressive multifocal leukoencephalopathy. |
| Multiple Sclerosis (MS) | | | | | |
| Genzyme/ Campath® (alemtuzumab) | For the treatment of B-cell CLL | For the treatment of relapsing-remitting MS | Binds to the CD52 antigen on B-cells and T-cells/ Therapeutic antibody | IV infusion | Completed enrollment in two phase III trials comparing Campath to Rebif® (interferon beta- 1a) in 2009. sBLA filing expected in 2011. |
| 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. Complete response letter October 2009. The FDA recommends an additional clinical trial. |

New Indications in the Pipeline (continued)

| Manufacturer/ Drug Name | Current Indication | Investigational Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|---|---|---|---|----------------------------|--|
| Oncology | | | | | |
| 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. |
| Pfizer/ Sutent® (sunitinib) | For the treatment of GIST and advanced RCC | For the treatment of breast cancer, NSCLC, hepatocellular cancer, HRPC and pancreatic cancer | Reduces tumor cell growth and blood supply/Multikinase inhibitor | Oral | Phase III trials ongoing. |
| Merck/ PegIntron® (peginterferon alfa-2b) | For the treatment of chronic HCV infection | For the adjuvant treatment of stage III melanoma | Unknown mechanism of action in cancer treatment/ Interferon | SC injection | sBLA filed September 2007. Complete response letter October 2009. |

New Indications in the Pipeline (continued)

| Manufacturer/ Drug Name | Current Indication | Investigational Indication | Mechanism of Action/Drug Class | Route of Administration | Comments |
|--|---|---|---|----------------------------|--|
| Transplantation | | | | | |
| Novartis/ Certican™ (everolimus) | For the treatment of advanced RCC in patients who have failed treatment with Sutent or Nexavar® | For the prevention of kidney transplant rejection in combination with Neoral® (cyclosporine) | Inhibits proliferation of T-cells/ mTOR inhibitor | Oral | NDA filed December 2002. First approvable letter October 2003. Second approvable letter August 2004. FDA advisory committee to review NDA in December 2009. Marketed under the brand name Afinitor for RCC indication. |

Glossary of Terms

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

Approvable letter – term used when assessing NDAs which indicated that a medication could probably be approved at a later date, provided that the applicant supplied requested information to the FDA or made specified changes. Since 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.

Cystic fibrosis – CF.

Double-blind trial – a type of study in which the participants and the investigators are blinded to treatment; this type of study has less bias than nonblinded studies.

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

Fast track 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.

Hereditary angioedema – HAE.

Multiple sclerosis – MS.

NDA – stands for “new drug application,” the process by which a manufacturer submits information to the FDA to gain approval for the agent; conducted after phase III development is completed.

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.

Pulmonary arterial hypertension – PAH.

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

Rheumatoid arthritis – RA.

Respiratory syncytial virus – RSV.

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 – Patients who have never been treated before for a particular condition.

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