

Specialty Pharmacy Pipeline Report

Fourth Quarter 2008

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.

Afinitor® (everolimus, RAD001)

Novartis has filed a New Drug Application (NDA) for Afinitor® for the treatment of advanced renal cell carcinoma (RCC) after failure to standard treatment. Current treatment options for advanced RCC include cytokines (interleukin-2 and interferon-alpha) or targeted therapies such as Sutent® (sunitinib), Nexavar® (sorafenib) and Torisel® (temsirolimus). Nexavar and Sutent are both orally administered multikinase inhibitors that prevent the growth and spread of cancer by slowing tumor growth and reducing the tumor's blood supply. Torisel specifically inhibits the mammalian target of rapamycin (mTOR) kinase, a protein that regulates tumor cell replication, growth and survival. Afinitor is also an mTOR inhibitor but is administered orally in contrast to Torisel, which is administered intravenously.

In a phase III study, Afinitor 10 mg once daily was compared to placebo for the treatment of patients with metastatic RCC who had failed Sutent, Nexavar or both medications. The median progression-free survival (PFS) was four months for patients in the Afinitor group and 1.9 months for patients in the placebo group. The PFS was considered significantly prolonged in the Afinitor group compared with the placebo group. The most common side effects in the Afinitor group were stomatitis, rash, fatigue or asthenia and diarrhea. In September 2008, the FDA granted priority review status to Afinitor's NDA for RCC.

In addition, phase III studies of Afinitor in combination with Sandostatin LAR® for the treatment of neuroendocrine tumors are ongoing.

Denosumab

Amgen is studying denosumab for the treatment of postmenopausal osteoporosis (PMO) and cancer-related bone loss. Osteoporosis is a skeletal disorder characterized by decreased bone strength which increases the risk of fracture. Primary osteoporosis is related to aging, with most cases occurring in postmenopausal women. Secondary osteoporosis is caused by chronic conditions or certain medications, including some treatments used for cancer. Denosumab is a fully human monoclonal antibody that inhibits RANKL (receptor activator of nuclear factor-kappa B ligand), an essential regulator of osteoclasts, which are the cells that break down bones.

In a phase III study, approximately 7,800 women ages 60 to 90 with osteoporosis were randomized to receive either a 60 mg subcutaneous (SC) injection of denosumab or a matching placebo every six months

for three years. Both groups of patients also received calcium and vitamin D supplements daily. During the study, 7.2 percent of placebo patients experienced a new vertebral fracture compared with 2.3 percent of denosumab patients. The difference in vertebral fracture rates was considered statistically significant for denosumab.

Another phase III study examined the effect of denosumab on bone mineral density (BMD) in women with nonmetastatic breast cancer who were receiving aromatase inhibitor therapy. Patients received denosumab (60 mg SC injection) or placebo every six months for two years. At month 12 (the primary endpoint), BMD at the lumbar spine increased significantly in the denosumab group, with a 5.5 percent difference from placebo. Denosumab was also studied in a phase III trial for the treatment of bone loss in more than 1,400 men undergoing androgen deprivation therapy for nonmetastatic prostate cancer. Patients in this trial received denosumab (60 mg SC injection) or placebo every six months for three years. Treatment with denosumab produced statistically significant greater increases in BMD at the lumbar spine compared with placebo.

In all three studies described above, the incidence and types of adverse events were similar between the denosumab and placebo groups.

Dirucotide (MBP8298)

Dirucotide, a synthetic human myelin basic protein developed by BioMS Medical and Eli Lilly, is an investigational medication in development for the treatment of secondary-progressive multiple sclerosis (SPMS), which is a phase of disease progression with or without relapses. 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. About 85 percent of patients with MS initially present with the relapsing-remitting form of the condition, characterized by episodic relapses, followed by remissions that may be partial or complete. Eventually, most of these patients will go on to develop SPMS. The remaining 15 percent of patients are diagnosed with primary-progressive or progressive-relapsing MS.

Disease-modifying therapies available for MS have been shown to reduce the frequency of relapses and

slow the accumulation of physical disability, but generally do not stop disease progression. Dirucotide is thought to act by inducing or restoring immunological tolerance to the ongoing immune attack caused by MS and may therefore reduce or prevent disease progression.

Patient recruitment for a phase III trial was completed in August 2008. In this trial, participants will receive either dirucotide or placebo intravenously every six months for two years. The primary endpoint of the trial is defined as a statistically and clinically significant increase in the time to progression of the disease. The FDA has granted fast track status for this trial.

Medications Recently Approved

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Approval Date	Comments
Hereditary Angioedema					
Lev Pharmaceuticals/ Cinryze™ (C1 inhibitor)	For routine prophylaxis against angioedema attacks in adolescent and adult patients with hereditary angioedema (HAE)	Replaces deficient C1 inhibitor/C1 inhibitor replacement therapy	IV infusion	10/10/08	First FDA-approved therapy for the prevention of HAE attacks. Lev has requested the withdrawal of the portion of the application referring to the acute treatment of HAE attacks. This data will be resubmitted as a supplemental Biologic License Application (sBLA).
Immune Thrombocytopenic Purpura					
Amgen/ Nplate™ (romiplostim)	For the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy	Stimulates the thrombopoietin receptor, which helps maintain platelet levels/ Thrombopoietin receptor agonist	SC injection	08/22/08	Nplate is only available through the Nplate NEXUS program, which consists of a patient registry and a requirement for prescribers to complete baseline and periodic safety information for every patient.

Pipeline Medications in Phase III Trials

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Amyloid A Amyloidosis				
BELLUS Health/ Kiacta™ (eprodisate), formerly Fibrillex™	For the treatment of amyloid A amyloidosis	Reduces amyloid protein deposition/ Amyloid fibrillogenesis inhibitor	Oral	Designated as an orphan drug. NDA filed February 2006. FDA granted priority review status April 2006. First approvable letter August 2006. Second approvable letter July 2007. NDA withdrawn March 2008. A second phase III trial was submitted for a Special Protocol Assessment (SPA). This trial is expected to begin fourth quarter of 2008.
Blood Disorder				
CSL Behring/ Human fibrinogen concentrate	For the treatment of congenital fibrinogen deficiency	Replaces deficient fibrinogen/Factor I	IV infusion	Designated as an orphan drug. Biologic License Application (BLA) filed July 2008. A response to the BLA is expected May 2009.
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 anticipated in 2008.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Blood Disorder				
GTC Therapeutics/ ATryn (antithrombin alfa)	For the prophylactic treatment of thromboembolisms in patients with hereditary antithrombin deficiency who are undergoing high-risk surgical and childbirth procedures	Replaces antithrombin/ Recombinant human antithrombin	SC injection	Designated as an orphan drug with fast track status. BLA filed August 2008. FDA granted priority review status September 2008. A response to the BLA is expected February 2009.
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	Phase III trial is being conducted under a SPA. NDA filing expected second half of 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 of 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.
Valeant Pharmaceuticals/ Viramidine® (taribavirin)	For the treatment of chronic HCV infection in combination with pegylated interferon alfa-2b	Reduces virus synthesis/Antiviral (synthetic nucleoside analogue)	Oral	Prodrug of ribavirin. Enrollment for a phase II trial using a weight-based dose of Viramidine initiated March 2007. Based on an early review of this study, Valeant will decide whether to begin a third phase III study at the weight-based dose.
Hereditary Angioedema				
CSL Behring/ Berinert® P (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 March 2008. A response to the BLA is expected January 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Hereditary Angioedema				
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. Dyax has requested priority review status.
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	BLA filing planned for the end of 2008.
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.
Immune Thrombocytopenic Purpura				
GlaxoSmithKline/ Promacta® (eltrombopag)	For the short-term treatment of previously treated patients with chronic ITP to increase platelet counts and reduce or prevent bleeding	Stimulates the proliferation and differentiation of megakaryocytes (bone marrow cells which give rise to platelets)/ Thrombopoietin-receptor agonist	Oral	NDA filed December 2007. FDA granted priority review status March 2008. A response to the NDA was originally expected in June 2008, then extended to September 2008; however, the FDA continues to review the NDA and has not released an expected timeframe for a response.
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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Inflammatory Diseases				
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. In August 2008, the FDA extended the review of the BLA to December 2008 to provide additional time for review of amendments provided by Centocor.
Novartis/ ACZ885	For the treatment of Muckle-Wells syndrome	Targets IL-1 β / IL-1 β inhibitor	SC injection	Designated as an orphan drug. BLA filing planned for 2009.
Roche and Chugai/ 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 related to the manufacturing of Actemra and other outstanding components, such as final labeling.
Multiple Sclerosis				
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 recruitment for phase III trial completed August 2008. FDA granted fast track status.
Novartis/ Fingolimod, formerly 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 the 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).
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 now expected in 2010 (previously planned for 2009).
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 now expected in the first half of 2009 (previously planned for 2008).
Cell Therapeutics/ Opaxio™ (paclitaxel poliglumex), formerly Xyotax™	For the treatment of advanced NSCLC in women	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 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				
Celtic Pharma and Neurobiological Technologies/ Xerecept® (corticotropin)	For the treatment of peritumoral brain edema	Reduces edema/ Synthetic human corticotropin releasing factor	SC injection	Designated as an orphan drug. NDA filing planned for 2008.
Cephalon/ Lestaurtinib	For the treatment of acute myeloid leukemia	Inhibits FMS-like tyrosine kinase-3 (FLT3) mutations/ FLT3 inhibitor	Oral	Designated as an orphan drug. NDA filing now expected in 2009 (previously planned for first half of 2008).
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 in mid-2009.
Genmab and GlaxoSmithKline/ HuMax-CD20® (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	Potential BLA filing in 2008.
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	NDA filed December 2005. Non-approvable letter December 2006. NDA amended June 2008. A response to the NDA is expected December 2008.
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.
Novartis/ Afinitor (everolimus, RAD001)	For the treatment of advanced RCC and neuroendocrine tumors	Inhibits tumor cell growth and the formation of new blood vessels/Antineoplastic (mammalian target of rapamycin inhibitor)	Oral	NDA for RCC filed July 2008. FDA granted priority review status September 2008.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
Protherics PLC/ Voraxaze™ (glucarpidase), formerly Carboxy-peptidase G2	Adjunctive therapy for cancer patients undergoing chemotherapy who are at risk for methotrexate (MTX) toxicity	Rapidly reduces serum MTX levels/ Recombinant enzyme	IV injection	Designated as an orphan drug with fast track status. BLA originally filed September 2006 and resubmitted November 2006. FDA requested additional information, and agreed to let Protherics resubmit its BLA as a rolling submission. Protherics plans to begin submitting a rolling BLA in the second half of 2008. Available through an expanded access program.
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	Primary endpoints were achieved in phase III studies for PMO and cancer- related bone loss.
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. Pfizer plans to begin an additional phase III study during the second half of 2008.
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), which is the current standard of care for the prevention of RSV. BLA filed January 2008. A response to the BLA is expected November 2008.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Transplant				
Genzyme/ Mozobil™ (plerixafor)	For the mobilization of stem cells for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma	Inhibits binding of stromal-derived factor 1 to chemokine receptor 4/ Chemokine receptor antagonist	SC injection	NDA filed June 2008. FDA granted priority review status September 2008. A response to the NDA is expected December 2008.
Novartis/ Certican™ (everolimus)	For the prevention of solid organ transplant rejection in combination with Neoral® (cyclosporine)	Inhibits T-cell proliferation, which are cells involved in the rejection process/ Immunosuppressant (mammalian target of rapamycin 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®.
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. Available through an expanded access program.

New Dosage Forms in the Pipeline (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Current Route of Administration	Investigational Route of Administration*	Comments
Cystic Fibrosis					
Novartis/ TBM100 (tobramycin)	For the treatment of patients with cystic fibrosis who have pulmonary <i>Pseudomonas aeruginosa</i>	Disrupts protein synthesis/ Aminoglycoside antibiotic	Solution for inhalation	Powder for inhalation	Expected to provide more rapid and convenient administration of tobramycin. NDA filing planned for 2009.
Multiple Sclerosis					
Merck Serono and Teva/ Mylinax® (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	FDA granted fast track status. Full enrollment for phase III study completed January 2007. Expected study completion November 2008.
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
Hepatitis					
Three Rivers Pharmaceuticals/ Infergen® (interferon alfacon-1)	For the treatment of HCV infection	For the treatment of chronic HCV in combination with ribavirin after failure to respond to previous course of pegylated interferon plus ribavirin	Inhibits viral replication/Interferon	SC injection	Clinical trials are ongoing.
Inflammatory Diseases					
Genentech and Biogen Idec/ Rituxan® (rituximab)	For the treatment of non-Hodgkin's lymphoma (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 and moderate to severe psoriasis	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	SC injection	BLA for the treatment of RA filed December 2007. UCB is evaluating further development or alternatives in psoriasis.
Oncology					
Cephalon/ Treanda® (bendamustine)	For the treatment of CLL	For the treatment of NHL in patients who failed Rituxan® (rituximab)	Causes cell death and disrupts cell division/Hybrid alkylating agent	IV infusion	NDA filed December 2007. A response to the NDA is expected October 2008.
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.
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)	Inhibits Bcr-Abl kinase/Tyrosine kinase inhibitor	Oral	supplemental New Drug Application (sNDA) filing anticipated in 2009.
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.
Schering- Plough/ 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 accepted and granted priority review status January 2008. FDA Advisory Committee postponed a planned review of the sBLA and requested clarification of existing data in March 2008. No new review date has been set.

New Indications in the Pipeline (continued)

Manufacturer/ Drug Name	Current Indication	Investigational Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
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.

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.

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*Information in the report is current as of October 2008, and was accessed on October 24, 2008.

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