

Specialty Pharmacy Pipeline Report

First 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 U.S. Food and Drug Administration (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. It also highlights selected, 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.

Nplate™ (romiplostim) and Promacta™ (eltrombopag)

Nplate™ and Promacta™ are two new medications in development for the treatment of immune (idiopathic) thrombocytopenic purpura (ITP). ITP is a condition in which antibodies not only cause an increase in platelet destruction, but may also cause a decrease in platelet production, resulting in thrombocytopenia (low platelet count). Platelets cause the blood to clot; therefore, when platelet levels are low, patients are at risk for bleeding events. Most patients with ITP experience minor bleeding symptoms, such as nosebleeds and bruising. In rare cases, major bleeding events, including intracranial hemorrhage, prolonged nosebleeds, and gastrointestinal bleeding may occur.

Information on the incidence and prevalence of ITP in the United States is limited. Recent studies in Europe

report that ITP occurs in five per 100,000 children and in two per 100,000 adults. In most children and some adults, ITP is an acute condition that resolves spontaneously within six months. In a small amount of children and most adults, ITP is a chronic condition that may require treatment. The main goals of therapy in ITP are to increase platelet count and prevent major bleeding events. Current treatment options include the use of corticosteroids, intravenous immunoglobulin, and anti-D immunoglobulin, which help prevent platelet destruction. The surgical removal of the spleen may be considered for patients who do not respond to these treatments.

Nplate is a thrombopoiesis-stimulating protein designed to increase platelet levels in adult patients with chronic ITP. In two phase III clinical trials, Nplate was administered as a weekly subcutaneous (SC) injection for 24 weeks and compared to placebo. The primary objective of the trial was to assess the efficacy of Nplate in achieving a durable platelet response, defined as a platelet count of at least 50×10^9 per liter during the last eight weeks of treatment. The durable platelet response in these trials was significantly higher in the Nplate groups (49 percent) compared with the placebo groups (2 percent). Nplate is designated as an orphan drug with fast track status. Amgen filed a Biologic License Application (BLA) in October 2007. The FDA granted priority review status to the application in January 2008, and Amgen expects a response to its BLA in the first half of 2008.

Promacta is a thrombopoietin-receptor agonist which has also been shown to increase platelet production. The use of once-daily Promacta in adult patients with chronic ITP, who had received at least one previous

treatment for ITP, was studied in a multicenter, randomized, double-blind, placebo-controlled trial. Patients were assigned to receive placebo or Promacta 30 mg, 50 mg, or 75 mg daily for up to six weeks. The primary endpoint of the study was a platelet count of 50,000 or more per cubic millimeter on day 43. The primary endpoint was achieved in 28 percent, 70 percent, and 81 percent of the patients in the Promacta 30 mg, 50 mg, and 75 mg groups, respectively, and in 11 percent of the patients in the placebo group. GlaxoSmithKline filed a New Drug Application (NDA) for Promacta in December 2007 and should receive a response to its NDA by October 2008.

Numax[®] (motavizumab)

Respiratory syncytial virus (RSV) infection causes respiratory tract illness in people of all ages, and is a serious public health problem around the world. In fact, RSV infection is the main cause of lower respiratory tract infections among infants and children, leading to the hospitalization of approximately 125,000 infants with severe infections each year.

Beyond symptom control, no effective treatments have been developed for RSV infection, so prevention is key. Synagis[®] (palivizumab), manufactured by MedImmune, is the only FDA-approved medication available for the prevention of RSV infection in high-risk infants. RespiGam[™] (RSV immune globulin intravenous) was also approved for this indication, but was discontinued at the end of 2003 due to Synagis entering the marketplace. Synagis is a monoclonal antibody that prevents RSV from infecting respiratory cells.

Numax[®] is a third generation anti-RSV product developed by MedImmune and AstraZeneca. Similar to Synagis, Numax is a monoclonal antibody administered through an intramuscular injection; however, it is expected to be more potent than Synagis. In one phase III trial, the efficacy of Numax versus Synagis was compared based on the incidence of RSV hospitalizations in each group. Although the incidence rate was low in both groups (Numax 1.4 percent, Synagis 1.9 percent), this difference was considered statistically significant. As a result, a BLA for Numax was filed in January 2008. The companies expect a response to their BLA by November 2008.

Albuferon[®] (albinterferon alfa-2b)

Albuferon[®] is a long-acting form of interferon alfa currently in phase III studies for the treatment of chronic hepatitis C virus (HCV) infection. The Centers for Disease Control and Prevention estimates that there are 3.2 million Americans chronically infected with HCV infection. Chronic infection with HCV can lead to liver cirrhosis, liver cancer, and liver failure. HCV is the most common indication for liver transplantation in the United States.

The current standard of treatment for chronic HCV infection is the use of a pegylated interferon alfa in combination with ribavirin. There are two pegylated interferons available in the United States, Pegasys[®] (peginterferon alfa-2a) and PegIntron[™] (peginterferon alfa-2b), which are each administered by a once weekly SC injection. Albuferon is a new form of interferon created by the genetic fusion of interferon alfa-2b to human albumin. The fusion of albumin to interferon causes Albuferon to remain in the body for a longer time than the pegylated interferons and is therefore administered once every other week.

In the two current phase III studies, therapy with Albuferon in combination with ribavirin is being compared to Pegasys in combination with ribavirin for the treatment of patients with chronic HCV infection who are treatment-naïve (patients who have never been treated for HCV before). One of the studies enrolled patients with genotype 1 HCV for 48 weeks of treatment, while the other study enrolled patients with genotype 2 or 3 HCV for 24 weeks of treatment. Human Genome Sciences and Novartis, the developers of Albuferon, expect to have all phase III data by the spring of 2009 and anticipate filing their BLA by fall of 2009.

Medications Recently Approved

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Approval Date	Comments
Crohn's Disease					
Elan and Biogen Idec/ Tysabri® (natalizumab)	For the treatment of adult patients with moderately to severely active Crohn's disease who have failed other therapies	Reduces the presence of white blood cells, which are involved in the inflammation process/Monoclonal antibody	IV infusion	01/14/08	Previously approved for the treatment of multiple sclerosis (MS). The companies anticipate that Tysabri will be available to Crohn's patients by the end of February 2008.
Growth Hormone					
Cangene/ Accretropin™ (somatropin rDNA origin)	For the treatment of pediatric patients who have growth failure due to an inadequate secretion of growth hormone, and for the treatment of short stature associated with Turner syndrome	Replaces growth hormone/Recombinant human growth hormone	SC injection	01/23/08	Third growth hormone to be approved as a follow-on protein product.
Human Immunodeficiency Virus (HIV)					
Tibotec Therapeutics and J&J/ Intelence™ (etravirine), formerly TMC125	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to a non-nucleoside reverse transcriptase inhibitor (NNRTI) and other antiretroviral agents	Inhibits viral DNA replication/NNRTI	Oral	01/18/08	First NNRTI that can be used in patients with NNRTI resistance.
Phenylketonuria					
BioMarin Pharmaceutical Inc./ Kuvan™ (sapropterin), formerly Phenoptin™	To reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia due to tetrahydrobiopterin-responsive Phenylketonuria (PKU) Kuvan must be used with a Phe-restricted diet	Enhances the activity of phenylalanine hydroxylase resulting in decreased Phe levels/Enzyme cofactor	Oral	12/31/07	Kuvan is the first medication approved specifically for the treatment of PKU.
Psoriasis					
Abbott/ Humira® (adalimumab)	For the treatment of moderate to severe chronic plaque psoriasis	Targets tumor necrosis factor (TNF) alpha, which is involved in the inflammation process/ Anti-TNF inhibitor	SC injection	01/18/08	Previously approved for the treatment of rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis, and Crohn's disease.

Pipeline Medications in Phase III Trials

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Amyloid A Amyloidosis				
Neurochem/ Kiacta™ (eprodiate), 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. The FDA accepted Neurochem's complete response to the July 2007 approvable letter. A response to the NDA is expected April 2008.
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. Phase III trials initiated July 2006. Full enrollment for first phase III study completed October 2007. Results from this study are expected mid-2008.
Hemophilia				
Wyeth/ ReFacto® AF (antihemophilic factor)	For the treatment of hemophilia	Blood clotting factor/ Recombinant factor VIII	Infusion	Launch anticipated in 2008.
Hepatitis				
Human Genome Sciences and Novartis/ Albupheron® (albinterferon alfa-2b)	In combination with ribavirin for the treatment of chronic 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.
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.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Immune Thrombocytopenic Purpura				
Amgen/ Nplate™ (romiplostim)	For the treatment of thrombocytopenia in adult patients with chronic ITP	Stimulates the thrombopoietin receptor, which helps maintain platelet levels/ Thrombopoiesis-stimulating protein	SC injection	Designated as an orphan drug with fast track status. BLA filed October 2007. FDA granted priority review status January 2008. A response to the BLA is expected in the first half of 2008.
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. A response to the BLA is expected October 2008.
Inflammatory Diseases				
Centocor and Schering-Plough/ Golimumab	For the treatment of RA, psoriatic arthritis, and ankylosing spondylitis	Targets TNF alpha, which is involved in the inflammatory process/ Anti-TNF inhibitor	SC injection	BLA filing planned for the first half of 2008.
Regeneron/ Riloncept (interleukin-1 trap)	For the treatment of cryopyrin-associated periodic syndrome	Binds and neutralizes interleukin-1 (IL-1)/ Long-acting IL-1 inhibitor	SC injection	Designated as an orphan drug with fast track status. BLA filed June 2007. FDA granted priority review status August 2007. In October 2007, Regeneron submitted additional information to the FDA, resulting in a three-month extension to the FDA's review period. A response to the BLA is now expected February 2008.
UCB/ Cimzia™ (certolizumab pegol)	For the treatment of moderate to severe or active Crohn's disease, moderate to severe or active RA, and moderate to severe psoriasis	Targets TNF alpha, which is involved in the inflammatory process/ Anti-TNF inhibitor	SC injection	BLA for the treatment of moderate to severe Crohn's disease filed March 2006. FDA requested more information December 2006. UCB will conduct a short-term efficacy study to confirm the induction of clinical response in Crohn's disease. Results from this study are expected in the second half of 2008. BLA for the treatment of RA filed December 2007.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Multiple Sclerosis				
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. Development for transplantation has been terminated for undisclosed reasons.
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).
Oncology				
Cell Therapeutics/ Xyotax™ (paclitaxel poliglumex)	For the treatment of advanced non-small cell lung cancer 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 Special Protocol Assessment (SPA) approval from the FDA for phase III trial September 2007. FDA granted fast track status.
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 planned for first half of 2008.
Cephalon/ Treanda® (bendamustine)	For the treatment of chronic lymphocytic leukemia (CLL) and for the treatment of non-Hodgkin's lymphoma (NHL) in patients who failed Rituxan® (rituximab)	Causes cell death and disrupts cell division/ Hybrid alkylating agent	IV infusion	Designated as an orphan drug for the treatment of CLL. NDA filed September 2007 for the treatment of CLL. FDA granted priority review status December 2007. A response to the NDA is expected March 2008. NDA filed December 2007 for the treatment of NHL.
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. Approvable 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. Dendreon anticipates an interim analysis of survival in the second half of 2008.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology				
Intarcia Therapeutics/ Atamestane	For first-line treatment of hormone-dependent breast cancer in combination with estrogen receptor blocker Fareston® (toremifene)	Interferes with estradiol production/ Steroidal aromatase inhibitor	Oral	Phase III studies ongoing.
Lorus Therapeutics/ Virulizin®	For first-line treatment of advanced pancreatic cancer in combination with Gemzar® (gemcitabine)	Increases the cytogenic effects of macrophages/ Biologic response modifier	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	FDA granted fast track status.
MGI PHARMA/ Saforis™ (glutamine in UpTec™)	For the prevention and treatment of chemotherapy-induced oral mucositis	Promotes healing and prevents damage to mucosa/Amino acid	Oral	NDA filed April 2006. FDA granted priority review status. Approvable letter October 2006. The FDA requested an additional phase III efficacy trial.
Novartis and Bayer Schering Pharma AG/ Vatalanib	For the treatment of metastatic colorectal cancer in combination with oxaliplatin, 5-FU, and leucovorin	Inhibits formation of blood vessels that supply nutrients to tumors/Tyrosine kinase inhibitor	Oral	NDA filing was planned for 2007, but did not take place for unknown reasons.
Protherics PLC/ Voraxaze™ (glucarpidase), formerly Carboxy- peptidase G2	Adjunctive therapy for cancer patients undergoing chemotherapy who are at risk for methotrexate toxicity	Rapidly reduces serum methotrexate 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 starting in the first 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 2009.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Osteoporosis				
Amgen/ Denosumab	For the treatment of postmenopausal osteoporosis (PMO) and treatment-induced bone loss	Inhibits bone destruction/ Monoclonal antibody	SC injection	All endpoints were met in the phase III trial for treatment-induced bone loss. Amgen anticipates completing a review of all the PMO data in the second half of 2008.
NPS Pharmaceuticals/ Preos [®] (parathyroid hormone)	For the treatment of PMO	Stimulates new bone growth/Recombinant human parathyroid hormone	SC injection	NDA filed May 2005. Approvable letter March 2006. Finalized the protocol design for a new phase IIIb clinical trial March 2007. After reviewing the development and commercialization options for Preos, NPS has decided to focus on hypoparathyroidism instead of PMO.
Psoriasis				
Centocor/ Ustekinumab	For the treatment of adult patients with chronic moderate to severe plaque psoriasis	Targets interleukin-12 and interleukin-23/ Dual interleukin inhibitor	SC injection	BLA filed December 2007. A response to the BLA is expected October 2008.
Pulmonary Arterial Hypertension				
Encysive Pharmaceuticals/ 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. Encysive filed a request with the FDA for formal dispute resolution to contest the third approvable letter August 2007. However, instead of pursuing the formal dispute resolution process, Encysive plans to conduct an additional phase III study.
Respiratory Syncytial Virus				
MedImmune and AstraZeneca/ Numax [®] (motavizumab)	For the prevention of 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.
Rheumatoid Arthritis				
Roche and Chugai/ Actemra [™] (tocilizumab)	For the treatment of RA	Blocks interleukin-6 receptors/Monoclonal antibody	IV infusion	BLA filed November 2007. A response to the BLA is expected September 2008.

Pipeline Medications in Phase III Trials (continued)

Manufacturer/ Drug Name	Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Transplant				
Biotest/ Anti-T-lymphocyte immune globulin (rabbit)	For the prevention of graft-versus-host disease in lung transplantation	Targets a range of antigens on activated T-cells/Polyclonal antibody	Injection	BLA filing expected early 2009. FDA granted fast track status.
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
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. A response to the NDA is expected September 2008. Available through an expanded access program.
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.
Oncology					
Xanthus Pharmaceuticals/ Fludarabine	For the treatment of relapsed B-cell CLL	Inhibits DNA synthesis/ Antineoplastic (purine nucleoside analogue)	IV infusion	Oral	Designated as an orphan drug. NDA accepted January 2008.
Pulmonary Arterial Hypertension					
United Therapeutics and Lung Rx/ Viveta (treprostinil)	For the treatment of PAH	Dilates pulmonary blood vessels/ Prostacyclin analog	SC or IV infusion	Inhalation	Studied in combination with Tracleer® (bosentan) or Revatio® (sildenafil).

*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
Crohn's Disease					
Bayer HealthCare Pharmaceuticals/ Leukine® (sargramostim)	To improve immune cell function in patients receiving treatment for myelogenous leukemia or following a bone marrow transplant	For the treatment of moderately to severely active Crohn's disease	Modulates immune system/Granulocyte macrophage colony stimulating factor	SC injection	
Hepatitis					
Gilead Sciences/ Viread® (tenofovir)	For the treatment of HIV	For the treatment of chronic hepatitis B virus infection	Inhibits the formation of viral DNA/ Nucleotide reverse transcriptase inhibitor	Oral	sNDA filed October 2007. A response to the sNDA is expected August 2008.
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.
Juvenile Rheumatoid Arthritis					
Abbott/ Humira® (adalimumab)	For the treatment of RA, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis	For the treatment of juvenile rheumatoid arthritis	Targets TNF alpha, which is involved in the inflammation process/ Anti-TNF inhibitor	SC injection	sBLA filed May 2007. A response to the sBLA is expected March 2008.
Amgen/ Kineret® (anakinra)	For the treatment of RA	For the treatment of polyarticular-course chronic juvenile rheumatoid arthritis	Blocks the biologic activity of IL-1/IL-1 inhibitor	SC injection	Clinical trials are ongoing.
Bristol-Myers Squibb/ Orencia® (abatacept)	For the treatment of moderate to severe RA in patients who have had an inadequate response to one or more disease- modifying anti- rheumatic drugs (DMARDs)	For the treatment of juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more DMARDs	Inhibits T-cell activation/Selective costimulation modulator	IV infusion	sBLA accepted August 2007.

New Indications in the Pipeline (continued)

Manufacturer/ Drug Name	Current Indication	Investigational Indication	Mechanism of Action/Drug Class	Route of Administration	Comments
Oncology					
Millennium Pharmaceuticals and J&J/ Velcade® (bortezomib)	For the treatment of multiple myeloma and mantle cell lymphoma in patients who have received at least one prior therapy	For the treatment of multiple myeloma in newly diagnosed patients	Interferes with the growth and survival of cancer cells/ Proteasome inhibitor	IV injection	sNDA filed December 2007. FDA granted priority review status January 2008. A response to the sBLA is expected June 2008.
Pfizer/ Sutent® (sunitinib)	For the treatment of gastrointestinal stromal tumor and advanced renal cell carcinoma	For the treatment of metastatic colorectal cancer	Reduces tumor cell growth and blood supply/Multikinase inhibitor	Oral	Phase III trial initiated June 2007.
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.
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	Stimulates bone formation/Parathyroid hormone analog	SC injection	sNDA filed February 2007.
Rheumatoid Arthritis					
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 anti-TNF inhibitors	For the treatment of moderately to severely active RA in biologic- naïve patients (patients who have not received a biologic medication for the treatment of RA before)	Reduces the amount of CD20-positive B-cells in the blood/Therapeutic antibody	IV infusion	The primary endpoint of the phase III trial was met January 2008.

Glossary of Terms

Approvable designation or letter – indicates that an FDA committee has reviewed the application and has suggested to the FDA that it approve the new medication. The FDA does not have to follow the advice of the committee, but usually does.

BLA – stands for “Biologic License Application,” similar to an NDA, but used for investigational medications that are considered to be biologic agents.

Double-blind – 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; usually applies to medications that treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

Follow-on protein product – generally refers to protein products that are intended to be similar enough to a product already on the market to permit the applicant to rely on certain existing scientific knowledge about the safety and effectiveness of the approved protein product for approval of the follow-on protein product.

Formal dispute resolution – an FDA process where sponsors can challenge regulatory decisions by bringing the dispute to the attention of FDA supervisors.

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.

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.

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.

Phase IIIb – trials that often begin before FDA approval. This phase—conducted after phase III trials—may supplement or complete earlier studies by providing additional safety data or they may test the approved medication for additional indications.

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.

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.

References

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www.cancer.org

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www.biopharminsight.com

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