PIPELINE REPORT
Fourth Quarter 2014

Information on recently approved, soon-to-be-approved and Phase 3 trial specialty medications

The Walgreens Pipeline Report provides a summary of the 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 3 studies that may impact treatment for certain specialty disease states or conditions. It also highlights select, recently approved or soon-to-be-approved specialty medications of interest to the marketplace. Drug information for approved products should be reviewed using the prescribing information (PI). For full PI, please refer to the DailyMed website. The medications with an asterisk indicate they have a boxed warning.

Note: This report is not intended for use by patients.

Walgreens

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.

Secukinumab

Novartis has filed a biologics license application (BLA) for secukinumab for the treatment of plaque psoriasis. Secukinumab is an interleukin-17A (IL-17A) inhibitor that interferes with the inflammatory response. In the double-blind, double-dummy, placebo-controlled Phase 3 FIXTURE trial, two doses of secukinumab (300 mg and 150 mg) were compared with Enbrel® (etanercept*) 50 mg and placebo. A total of 1,306 patients with moderate-to-severe plaque psoriasis were randomized to one of four treatment groups: secukinumab 150 mg and placebo Enbrel, secukinumab 300 mg and placebo Enbrel, placebo secukinumab and Enbrel 50 mg or placebo secukinumab and placebo Enbrel. Secukinumab and secukinumab placebo were administered as a subcutaneous injection once weekly for five weeks, then every four weeks thereafter. Enbrel and Enbrel placebo were administered as a subcutaneous injection twice weekly for 12 weeks, then once weekly thereafter.

The coprimary endpoints of the trial were the proportion of patients who had a reduction of 75 percent or more from baseline in the psoriasis area-and-severity index score (PASI 75) and a score of 0 (clear) or 1 (almost clear) on a 5-point modified investigator's global assessment (IGA) as compared to placebo after 12 weeks of treatment. Secondary endpoints included the proportion of patients who had a PASI 75 and a score of 0 or 1 on the modified IGA as compared to Enbrel after 12 weeks of treatment.

The proportion of patients achieving a PASI 75 at week 12 was 77.1 percent with secukinumab 300 mg, 67 percent with secukinumab 150 mg, 44 percent with Enbrel, and 4.9 percent with placebo. The proportion of patients with a score of 0 or 1 on the modified IGA at week 12 was 62.5 percent with secukinumab 300 mg, 51.1 percent with secukinumab 150 mg, 27.2 percent with Enbrel, and 2.8 percent with placebo. The differences in the proportion of patients achieving a PASI 75 and a score of 0 or 1 on the modified IGA were statistically significantly higher for both doses of secukinumab as compared to placebo or Enbrel. The rates of infection were higher with secukinumab than with placebo but were similar to those with Enbrel. The BLA for secukinumab was filed in October 2013, with a response expected in January 2015.

Palbociclib

Palbociclib is an investigational, orally administered, cyclin-dependent kinase inhibitor which helps prevent tumor cell progression. The FDA granted palbociclib breakthrough therapy designation for the potential treatment of patients with breast cancer.

PALOMA-1 was a two-part Phase 2 trial evaluating the use of palbociclib for the treatment of postmenopausal women with estrogen receptor positive (ER+) and human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer. In both parts of the trial, patients were randomized to receive palbociclib (125 mg by mouth once daily for 21 days of a 28-day cycle) in combination with letrozole (2.5 mg by mouth once daily) or letrozole alone. In part 1 of the trial, 66 patients with ER+/HER2- advanced breast cancer were randomized while part 2 of the trial randomized an additional 99 patients whose tumors were selected for the presence of certain biomarkers including cyclin D1 amplification/p16 loss. The primary endpoint of both parts of the trial was progression-free survival (PFS). The median PFS was 20.2 months in the palbociclib and letrozole group compared to 10.2 months in the letrozole alone group. This difference was considered to be statistically significant. The most common treatment-related adverse events reported in the combination group were neutropenia, leukopenia, anemia and fatigue.

Two double-blind Phase 3 trials of palbociclib in advanced/metastatic breast cancer have been initiated. PALOMA-2 is evaluating palbociclib in combination with letrozole versus letrozole alone as a first-line treatment for post-menopausal women with ER+/HER2- advanced breast cancer. PALOMA-3 is evaluating palbociclib in combination with Faslodex® (fulvestrant) versus Faslodex alone in women with hormone receptor-positive (HR+), HER2- metastatic breast cancer whose disease has progressed after prior endocrine therapy. Based on the results of PALOMA-1, Pfizer filed a new drug application (NDA) in August 2014.

Mepolizumab

GlaxoSmithKline developed mepolizumab for the treatment of severe eosinophilic asthma. Eosinophils are a type of white blood cell which accumulate during allergic reactions, including allergic asthma. Interleukin-5 (IL-5) is an essential signal for the movement of eosinophils from the bone marrow into the lung. Mepolizumab is an IL-15 inhibitor which interferes with the inflammatory response.

In a Phase 3, double-blind, double-dummy, placebo-controlled trial, 576 patients with severe asthma, who had experienced frequent exacerbations despite treatment with high-dose inhaled corticosteroids plus at least one other controller medication were enrolled. All patients were also required to have a blood eosinophil count above a pre-specified threshold of ≥150 cells/µl at initiation of treatment or who had blood eosinophils ≥300 cells/µl in the past 12 months to be eligible for the trial. Patients were randomized in a 1:1:1 ratio to receive one of the following treatments every four weeks for a total of eight doses: mepolizumab 75 mg intravenously (IV) and placebo subcutaneously, mepolizumab 100 mg subcutaneously and placebo IV, or placebo IV and placebo subcutaneously. The primary endpoint of the trial was reduction in the frequency of clinically significant asthma exacerbations.

Mepolizumab IV demonstrated a 47 percent reduction in exacerbations and mepolizumab subcutaneous demonstrated a 53 percent reduction in exacerbations compared to placebo. These reductions were considered to be statistically significant. The most common adverse events reported across all treatment groups were nasopharyngitis, headache, upper respiratory tract infection and asthma. GlaxoSmithKline is planning to file a BLA for mepolizumab by the end of 2014.

Medications recently approved

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Approval date	Comments
Blood disorders					
GlaxoSmithKline/Promacta® (eltrombopag*)	For the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy	Thrombopoietin receptor agonist	Oral	8/26/14	• Previously approved for the treatment of thrombocytopenia in patients with chronic immune thrombocytopenia or with chronic hepatitis C virus (HCV) to allow the initiation and maintenance of interferon-based therapy
Cancer					
Genentech/Avastin® (bevacizumab*)	In combination with paclitaxel and cisplatin or paclitaxel and topotecan for the treatment of persistent, recurrent or metastatic carcinoma of the cervix	Reduces tumor cell growth and blood supply/Vascular endothelial growth factor (VEGF) inhibitor	IV infusion	8/14/14	• Previously approved for the treatment of colorectal cancer, non-small cell lung cancer (NSCLC), glioblastoma, and renal cell carcinoma (RCC)
Medivation and Astellas Pharma/Xtandi® (enzalutamide)	For use in men with metastatic castration-resistant prostate cancer (CRPC) who have not received chemotherapy	Inhibits cell growth and survival/Androgen receptor inhibitor	Oral	9/10/14	• Previously approved for use in patients with metastatic CRPC who previously received docetaxel*
Merck/ Keytruda® (pembrolizumab)	For the treatment of patients with unresectable or metastatic melanoma (MM) and disease progression following Yervoy (ipilimumab) and, if BRAF V600 mutation positive, a BRAF inhibitor	Activates immune system to target cancer cells/Programmed cell death 1 (PD-1) checkpoint inhibitor	IV infusion	9/4/14	• First PD-1 checkpoint inhibitor approved
Human immunodeficiency virus					
ViiV Healthcare/Triumeq® (abacavir,* dolutegravir, lamivudine*)	For the treatment of human immunodeficiency virus type 1 (HIV-1) infection	Prevents virus replication/Integrase strand transfer inhibitor (INSTI) and nucleoside reverse transcriptase inhibitors (NRTIs)	Oral	8/22/14	• First approved dolutegravir-based fixed-dose combination
Lysosomal storage diseases					
Genzyme/Cerdelga™ (eliglustat)	For the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers as detected by an FDA-cleared test	Reduces the production of glucosylceramide/ Glucosylceramide synthase inhibitor	Oral	8/19/14	• Only first-line oral therapy approved for certain adult Gaucher disease type 1 patients
Multiple sclerosis					
Biogen Idec/Plegridy™ (peginterferon beta-1a)	For the treatment of patients with relapsing forms of multiple sclerosis (MS)	Unknown mechanism of action in MS/ Interferon	Subcutaneous injection	8/15/14	• First pegylated interferon beta approved for this indication

*These medications have a boxed warning.

Medications recently approved (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Approval date	Comments
Ophthalmology					
Regeneron Pharmaceuticals/ Eylea® (aflibercept)	For the treatment of diabetic macular edema (DME)	Binds vascular endothelial growth factor and placental growth factor/Antiangiogenesis inhibitor	Intravitreal injection	7/29/14	• Previously approved for the treatment of neovascular (wet) age-related macular degeneration (AMD) and macular edema following central retinal vein occlusion (CRVO)
Primary immunodeficiency					
Baxter/HyQvia (immune globulin infusion 10% [human] with recombinant human hyaluronidase)	For the treatment of primary immunodeficiency (PI) in adults	Replaces deficient immune globulin (IG)/ Replacement therapy	Subcutaneous infusion	9/12/14	• First subcutaneous IG treatment approved for PI patients with a dosing regimen requiring only one infusion up to once per month (every three to four weeks) and one injection site per infusion to deliver a full therapeutic dose of IG

Pipeline medications in Phase 3 trials

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Asthma				
GlaxoSmithKline/Mepolizumab	For the treatment of severe eosinophilic asthma	Interferes with the inflammatory response/IL-15 inhibitor	IV infusion or subcutaneous injection	• Primary endpoint achieved in two Phase 3 trials March 2014 • BLA filing planned for 2014
Bleeding disorders				
Baxter/BAX 111 (recombinant von Willebrand factor)	For the treatment of bleeding in patients with von Willebrand disease	Promotes blood clotting/Factor replacement therapy	IV infusion	• Designated as an orphan drug • Primary endpoint achieved in Phase 3 trial April 2014 • BLA filing planned for 2014
Baxter/BAX 855 (recombinant factor VIII)	For the treatment and prevention of bleeding in patients with hemophilia A	Promotes blood clotting/Factor replacement therapy	IV infusion	• Phase 3 trial met primary endpoint August 2014 • BLA filing planned by the end of 2014
Baxter/OBI-1 (recombinant antihemophilic porcine sequence factor VIII)	For the treatment of bleeding in patients with acquired hemophilia A	Promotes blood clotting/Factor replacement therapy	IV infusion	• Designated as an orphan drug with fast-track status • BLA filed December 2013
Cancer				
Amgen/Blinatumomab	For the treatment of Philadelphia-negative relapsed/refractory B-precursor acute lymphoblastic leukemia	Activates immune system to target cancer cells/Bispecific T cell engager (BiTE®) antibody	IV infusion	• Designated as an orphan drug • FDA granted breakthrough therapy designation • BLA filing planned for 2014
AstraZeneca, MedImmune/ Lynparza (olaparib)	For the treatment of platinum sensitive relapsed ovarian cancer patients who have a breast cancer (*BRCA*) mutation	Inhibits cell growth and survival/Poly ADP-ribose polymerase (PARP) inhibitor	Oral	• Designated as an orphan drug • NDA accepted and granted priority review April 2014 • FDA advisory committee did not recommend accelerated approval June 2014 • Major amendment to NDA submitted July 2014 • A response to the NDA is expected January 2015
Bristol-Myers Squibb/Opdivo (nivolumab)	For the third-line treatment of squamous cell NSCLC	Activates immune system to target cancer cells/PD-1 checkpoint inhibitor	IV injection	• FDA granted fast-track status • Initiated rolling BLA submission April 2014; expecting to complete the application by the end of 2014
CTI BioPharma/Opaxio (paclitaxel poliglumex)	For the treatment of ovarian cancer	Inhibits cell division/ Microtubule inhibitor	IV infusion	• Links paclitaxel to a biodegradable polyglutamate polymer that delivers more chemotherapy to tumor cells • Completed enrollment of Phase 3 trial January 2014
CTI BioPharma/Pacritinib	For the treatment of myelofibrosis (MF)	Inhibits the formation and development of blood cells/Tyrosine kinase inhibitor (TKI)	Oral	• FDA granted fast-track status • Top-line results from Phase 3 trial expected in 2015

Pipeline medications in Phase 3 trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Cancer				
Eisai/Lenvatinib	For the treatment of progressive radioiodine-refractory differentiated thyroid cancer	Inhibits cell growth and survival/TKI	Oral	• Designated as an orphan drug • NDA filed August 2014
Eli Lilly/Necitumumab	For the treatment of metastatic squamous NSCLC	Reduces tumor cell growth and blood supply/Epidermal growth factor receptor inhibitor	IV infusion	• Primary endpoint achieved in Phase 3 trial • Filing anticipated by the end of 2014
Novartis/Binimetinib	For the treatment of neuroblastoma RAS viral (v-ras) oncogene homolog (NRAS) mutant melanoma	Inhibits cell growth and survival/ Mitogen-activated protein kinase (MEK) inhibitor	Oral	• Designated as an orphan drug • Regulatory filings planned for 2015
Novartis/Midostaurin	For treatment of patients with FLT-3 mutated acute myeloid leukemia (AML)	Inhibits cell growth and survival/ Signal transduction inhibitor	Oral	• Designated as an orphan drug • Regulatory filings planned for 2015
Novartis/Panobinostat	In combination with Velcade® (bortezomib) and dexamethasone for the treatment of relapsed or refractory MM	Inhibits cell growth and survival/Histone deacetylase inhibitor	Oral	• Designated as an orphan drug • NDA accepted and granted priority review May 2014
Pfizer/Palbociclib	In combination with letrozole for the treatment ER+, HER2- advanced breast cancer who have not received previous systemic treatment	Prevents tumor cell progression/ Cyclin-dependent kinase inhibitor	Oral	• FDA granted breakthrough therapy designation • NDA filed August 2014
Puma Biotechnology/Neratinib	For the extended adjuvant treatment of breast cancer	Inhibits cell growth and survival/TKI	Oral	• Primary endpoint achieved in Phase 3 trial July 2014 • Regulatory filings planned for first half 2015
Cystic fibrosis				
Vertex Pharmaceuticals/ Lumacaftor (VX-809)	In combination with Kalydeco® (ivacaftor) in patients with cystic fibrosis (CF) who have two copies of the F508del mutation in the cystic fibrosis transmembrane conductance regulator *(CFTR)* gene	Increases the movement of *CFTR* to the cell surface/*CFTR* corrector	Oral	• Designated as an orphan drug • FDA granted breakthrough therapy designation • NDA filing planned for fourth quarter 2014
Endocrine disorders				
NPS Pharmaceuticals/Natpara (recombinant human parathyroid hormone)	For the treatment of hypoparathyroidism	Replaces deficient hormone/ Hormone replacement therapy	Subcutaneous injection	• Designated as an orphan drug • BLA filed October 2013 • A response to the BLA is expected October 2014

Pipeline medications in Phase 3 trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Fertility				
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	Subcutaneous injection	• NDA accepted for standard review September 2013 • Received complete-response letter July 2014
Growth disorders				
Aeterna Zentaris/Macrilen (macimorelin acetate)	For the evaluation of adult growth hormone deficiency	Stimulates the secretion of growth hormone/Ghrelin receptor agonist	Oral	• Designated as an orphan drug • NDA filed November 2013 • A response to the NDA is expected November 2014
Hepatitis				
AbbVie/ABT-450 + ritonavir* ombitasvir (ABT-267) dasabuvir (ABT-333)	In combination with ribavirin for the treatment of HCV infection in genotype 1 patients	Prevents virus replication/Protease inhibitor (ABT-450 + ritonavir), NS5A inhibitor (ABT-267), non-nucleoside polymerase inhibitor (ABT-333)	Oral	• FDA granted breakthrough therapy designation • NDA filed April 2014 • FDA granted priority review status • A response to the NDA is expected December 2014
Bristol-Myers Squibb/Daclatasvir and asunaprevir	For the treatment of chronic HCV infection in genotype 1b patients	Prevents virus replication/NS5A inhibitor (daclatasvir), NS3 inhibitor (asunaprevir)	Oral	• FDA granted breakthrough therapy designation • NDA filed March 2014 • FDA granted priority review status • A response to the NDA is expected November 2014
Bristol-Myers Squibb/Daclatasvir	In combination with other agents for the treatment of chronic HCV infection	Prevents virus replication/NS5A inhibitor	Oral	• NDA filed March 2014
Gilead Sciences/Ledipasvir	In fixed-dose combination with Sovaldi® (sofosbuvir) for the treatment of chronic HCV infection in genotype 1 patients	Prevents virus replication/NS5A inhibitor	Oral	• FDA granted breakthrough therapy designation • NDA filed February 2014 • FDA granted priority review status • A response to the NDA is expected October 2014

*These medications have a boxed warning.

Pipeline medications in Phase 3 trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Human immunodeficiency virus				
Gilead Sciences/Cobicistat	To increase blood levels of certain protease inhibitors to enable once-daily dosing	Inhibits cytochrome P4503A/ Pharmacoenhancer	Oral	• NDA filed June 2012 • Received complete -response letter April 2013 • FDA accepted resubmission of NDA April 2014 • A response to the NDA is expected October 2014
Gilead Sciences/Elvitegravir	For the treatment of human immunodeficiency virus (HIV) infection in treatment-experienced patients	Prevents virus replication/Integrase inhibitor	Oral	• NDA filed June 2012 • Received complete response letter April 2013 • FDA accepted resubmission of NDA April 2014 • A response to the NDA is expected October 2014
Immune Response BioPharma/ Remune	To boost the immune system in HIV patients receiving antiviral treatment	Induces an HIV-specific T-cell response/Therapeutic vaccine	Intramuscular (IM) injection	• Designated as an orphan drug for pediatric patients • Planning a new Phase 2 trial
Hypercholesterolemia				
Amgen/Evolocumab	For the treatment of hypercholesterolemia	Increases the removal of low-density lipoprotein cholesterol from the blood/Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor	Subcutaneous injection	• Designated as an orphan drug for the treatment of homozygous familial hypercholesterolemia • BLA filed August 2014
Sanofi and Regeneron Pharmaceuticals/Alirocumab	For the treatment of hypercholesterolemia	Increases the removal of low-density lipoprotein cholesterol from the blood/PCSK9 inhibitor	Subcutaneous injection	• Primary endpoint achieved in nine Phase 3 trials July 2014 • BLA filing planned for 2014
Inflammatory diseases				
Eli Lilly/Ixekizumab	For the treatment of plaque psoriasis	Interferes with the inflammatory response/IL-17 inhibitor	Subcutaneous injection	• Primary endpoint achieved in three Phase 3 trials August 2014 • BLA filing planned for first half 2015
Novartis/Secukinumab (AIN457)	For the treatment of plaque psoriasis	Interferes with the inflammatory response/IL-17A inhibitor	Subcutaneous injection	• BLA filed October 2013 • A response to the BLA is expected January 2015
Sanofi and Regeneron Pharmaceuticals/Sarilumab	For the treatment of rheumatoid arthritis (RA)	Interferes with the inflammatory response/IL-16 inhibitor	Subcutaneous injection	• Coprimary endpoints achieved in Phase 3 trial November 2013 • Six Phase 3 trials ongoing

Pipeline medications in Phase 3 trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Lambert Eaton myasthenic syndrome				
Catalyst Pharmaceutical Partners/ Firdapse (amifampridine phosphate)	For the treatment of symptoms associated with Lambert-Eaton myasthenic syndrome	Improves impulse conduction in nerve fibers/Potassium channel blocker	Oral	• Designated as an orphan drug • FDA granted breakthrough therapy designation • Phase 3 results are expected by end of 2014
Lysosomal storage diseases				
Amicus Therapeutics and GlaxoSmithKline/Amigal (migalastat HCl)	For the treatment of Fabry disease	Binds to and stabilizes alpha-galactosidase/Alpha-galactosidase A enhancer	Oral	• Designated as an orphan drug • Primary endpoint achieved in stage 2 of first Phase 3 trial April 2014 • Co-primary endpoints achieved in second Phase 3 trial August 2014
Synageva BioPharma/ Sebelipase alfa	For the treatment of early and late onset lysosomal acid lipase (LAL) deficiency	Replaces deficient LAL/Enzyme replacement therapy	IV infusion	• Designated as an orphan drug with fast-track status • FDA granted breakthrough therapy designation for early onset LAL deficiency • Primary endpoint achieved in Phase 3 trial June 2014 • BLA filing planned for first quarter 2015
Metabolic disorders				
Alexion Pharmaceuticals/ Asfotase alfa	For the treatment of hypophosphatasia	Normalizes the genetically defective metabolic process/Targeted enzyme replacement therapy	Subcutaneous injection	• Designated as an orphan drug with fast-track status • FDA granted breakthrough therapy designation • Initiated rolling BLA submission April 2014
Multiple sclerosis				
Teva Pharmaceuticals/Laquinimod	For the treatment of relapsing-remitting MS	Inhibits autoimmune and inflammatory disease activity/ Immunomodulatory agent	Oral	• Third Phase 3 trial is ongoing, results are expected 2016 • This trial is being conducted under a special protocol assessment
Muscular dystrophy				
Prosensa Holding N.V./Drisapersen	For the treatment of Duchenne muscular dystrophy (DMD)	Enables production of a functional dystrophin protein/Exon skipping therapy	Subcutaneous injection	• Designated as an orphan drug • FDA granted breakthrough therapy designation • NDA filing planned for fourth quarter 2014
Sarepta Therapeutics/Eteplirsen	For the treatment of DMD	Enables production of a functional dystrophin protein/Exon skipping therapy	IV infusion	• Designated as an orphan drug with fast-track status • NDA filing planned by end of 2014

Pipeline medications in Phase 3 trials (continued)

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Route of administration	Comments
Pulmonary fibrosis				
Boehringer Ingelheim/Nintedanib	For the treatment of idiopathic pulmonary fibrosis (IPF)	Targets growth factors/TKI	Oral	• Designated as an orphan drug with fast-track status • FDA granted breakthrough therapy designation • NDA accepted and granted priority review July 2014
InterMune/Pirfenidone	For the treatment of IPF	Suppresses fibrosis and inflammation/Anti-fibrotic agent	Oral	• Designated as an orphan drug with fast-track status • FDA granted breakthrough therapy designation • Received a complete response letter May 2010 • Resubmitted NDA May 2014 • A response to the NDA is expected November 2014
Pulmonary hypertension				
Actelion/Selexipag	For the treatment of pulmonary arterial hypertension (PAH)	Reduces vascular smooth muscle constriction/Prostacyclin receptor agonist	Oral	• Designated as an orphan drug • Primary endpoint achieved in Phase 3 trial June 2014

New dosage forms in the pipeline

Manufacturer/ Drug name	Indication	Mechanism of action/ Drug class	Current route of administration	Investigational route of administration†	Comments
Multiple sclerosis					
Biogen Idec and AbbVie/ Daclizumab HYP (high-yield process)	For the treatment of relapsing-remitting MS	Binds to the CD25 receptor on T-cells/ Therapeutic antibody	IV infusion	Subcutaneous injection	• Primary endpoint achieved in Phase 3 trial June 2014 • Previously marketed as Zenapax® (daclizumab*) for the prevention of acute kidney rejection
Neuroendocrine disorders					
Novartis/Signifor LAR (pasireotide long-acting release)	For the treatment of acromegaly	Binds somatostatin receptors/Somatostatin analogue	Subcutaneous injection	IM injection	• Monthly IM injection • Primary endpoint achieved in Phase 3 trial July 2013 • NDA filed fourth quarter 2013

*These medications have a boxed warning.
†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
Cancer					
Celgene/Revlimid® (lenalidomide*)	For the treatment of previously treated MM, myelodysplastic syndromes and relapsed or refractory mantle cell lymphoma	For the treatment of newly diagnosed MM	Possesses immunomodulatory, anti-inflammatory and antiangiogenic properties/Thalidomide analogue	Oral	• Primary endpoint achieved in Phase 3 trial July 2013 • sNDA filed April 2014 • A response to the sNDA is expected February 2015
Eli Lilly/Cyramza™ (ramucirumab*)	For the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy	In combination with paclitaxel for the treatment of second-line gastric cancer In combination with chemotherapy for the second-line treatment of NSCLC	Reduces tumor cell growth and blood supply/VEGFR2 antagonist	IV infusion	• sBLA for second-line gastric cancer indication filed June 2014 • A response to the sBLA is expected March 2015 • Primary endpoint achieved in Phase 3 NSCLC trial February 2014 • First regulatory filing for NSCLC indication planned for second half 2014
Genentech/Avastin® (bevacizumab*)	For the treatment of metastatic colorectal cancer, non-squamous NSCLC, glioblastoma, metastatic RCC, and metastatic carcinoma of the cervix	In combination with chemotherapy for the treatment of women with recurrent platinum-resistant ovarian cancer	Reduces tumor cell growth and blood supply/Vascular endothelial growth factor (VEGF) inhibitor	IV infusion	• sBLA accepted and granted priority review July 2014 • A response to the sBLA is expected November 2014
Incyte Corporation/ Jakafi® (ruxolitinib)	For the treatment of patients with intermediate or high-risk MF, including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF	For the treatment of polycythemia vera in patients who are resistant to or intolerant of hydroxyurea	Inhibits the formation and development of blood cells/JAK inhibitor	Oral	• Designated as an orphan drug with fast-track status • sNDA accepted and granted priority review August 2014 • A response to the sNDA is expected December 2014
Ipsen/Somatuline® Depot (lanreotide)	For the long-term treatment of acromegalic patients who have had an inadequate response to surgery/ radiotherapy, or for whom surgery/ radiotherapy is not an option	For the treatment of gastroenteropancreatic neuroendocrine tumors	Binds somatostatin receptors/Somatostatin analogue	Subcutaneous injection	• sNDA filed July 2014 • FDA granted priority review status • A response to the sNDA is expected first quarter 2015
Cystic fibrosis					
Vertex Pharmaceuticals/ Kalydeco® (ivacaftor)	For the treatment of CF in patients age 6 years and older who have one of the following mutations in the *CFTR* gene: *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N*, or *S549R*	For the treatment of CF patients ages 18 and older who have the R117H mutation in the *CFTR* gene	Increases chloride ion transport across cell membranes/*CFTR* potentiator	Oral	• Supplemental new drug application (sNDA) filed June 2014

*These medications have a boxed warning.

New indications in the pipeline (continued)

Manufacturer/ Drug name	Current indication	Investigational indication	Mechanism of action/ Drug class	Route of administration	Comments
Inflammatory diseases					
AbbVie/Humira® (adalimumab*)	For the treatment of RA, polyarticular juvenile idiopathic arthritis, psoriatic arthritis (PsA), ankylosing spondylitis, Crohn's disease (CD), ulcerative colitis (UC) and psoriasis	For the treatment of hidradenitis suppurativa	Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor	Subcutaneous injection	• Results from Phase 3 trials are expected 2014
Celgene/Otezla® (apremilast)	For the treatment of adult patients with active PsA	For the treatment of psoriasis	Modulates the inflammatory response/ Phosphodiesterase 4 inhibitor	Oral	• NDA filed September 2013 • A response to the NDA is expected September 2014
Pfizer/Xeljanz® (tofacitinib*)	For the treatment of RA	For the treatment of moderate-to-severe chronic plaque psoriasis	Interferes with the inflammatory and immune responses/Janus kinase (JAK) inhibitor	Oral	• sNDA filing planned for 2015
Multiple sclerosis					
Genzyme/Lemtrada (alemtuzumab*)	For the treatment of B-cell chronic lymphocytic leukemia (CLL)	For the treatment of relapsing MS	Binds to the CD52 antigen on B-cells and T-cells/Therapeutic antibody	IV injection	• FDA granted fast-track status • Supplemental biologics license application (sBLA) filed June 2012 • Received a complete response letter December 2013 • FDA accepted sBLA resubmission for review May 2014 • A response to the sBLA is expected fourth quarter 2014 • Marketed as Campath® for CLL indication
Ophthalmology					
Genentech/Lucentis® (ranibizumab)	For the treatment of neovascular (wet) AMD, macular edema following retinal vein occlusion and DME	For the treatment of diabetic retinopathy	Binds vascular endothelial growth factor/Antiangiogenesis inhibitor	Intravitreal injection	• sBLA filed August 2014
Regeneron Pharmaceuticals/ Eylea® (aflibercept)	For the treatment of neovascular (wet) AMD, macular edema following CRVO and DME	For the treatment of macular edema following branch retinal vein occlusion	Binds vascular endothelial growth factor and placental growth factor/ Antiangiogenesis inhibitor	Intravitreal injection	• sBLA accepted February 2014 • A response to the sBLA expected October 2014

*These medications have a boxed warning.

New biosimilars in the pipeline

Manufacturer/ Drug name	Reference Manufacturer/Product	Investigational indication	Mechanism of action/ Drug class	Route of administration	Comments
Cancer					
Sandoz/Filgrastim	Amgen/Neupogen (filgrastim)	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever	Stimulates production of neutrophils/Granulocyte colony-stimulating factor	Subcutaneous injection, IV infusion, or subcutaneous infusion	• BLA accepted July 2014

Glossary of terms

BLA

Stands for "biologics license application," similar to an NDA but used for investigational medications that are considered to be biologic agents.

Breakthrough therapy designation

Intended to expedite the development and review of a potential new drug for serious or life-threatening diseases.

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.

Fast track

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 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 3 development is completed.

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 2

Second phase of medication development: may involve a few dozen to a couple hundred patients to determine safety and preliminary data on efficacy.

Phase 3

Last phase of medication development; involves safety and efficacy trials of the new medication. This phase of development can take years to complete.

Glossary of terms (continued)

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.

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 biologics 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.

References

Articles:

Finn RS, Crown JP, Lang I, et al. Results of a randomized phase 2 study of PD 0332991, a cyclin-dependent kinase (CDK) 4/6 inhibitor, in combination with letrozole vs letrozole alone for first-line treatment of ER+/HER2– advanced breast cancer (BC). *Cancer Res* 2012;72(24 Suppl):Abstract nr S1-6.

Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis – results of two phase 3 trials. *N Engl J Med* 2014;371:326-338.

Websites:

ClinicalTrials—clinicaltrials.gov

DailyMed—dailymed.nlm.nih.gov

EvaluatePharma—evaluategroup.com

Manufacturers' websites

U.S. Food and Drug Administration—fda.gov

Information in the report is current as of September 2014 and was accessed on September 12, 2014.

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