Pipeline Report

Information on recently approved, soon to be approved and phase III trial specialty medications.

First quarter 2014

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 III 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 PI (prescribing information). For full PI, please refer to the DailyMed website. The medications with an asterisk indicate they have a boxed warning.

This report is not intended to be used by patients.

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.

Ramucirumab
Eli Lilly has filed a biologics license application (BLA) for ramucirumab as a single-agent treatment for advanced gastric cancer following disease progression after initial chemotherapy. Ramucirumab is a vascular endothelial growth factor (VEGF) receptor inhibitor that reduces tumor cell growth and blood supply.

The BLA filing was based on a randomized, double-blind, phase III trial. Patients who had failed a first-line chemotherapy treatment were enrolled and assigned to receive ramucirumab (238 patients) or placebo (117 patients). Ramucirumab was administered as an intravenous (IV) infusion at a dose of 8 mg/kg every two weeks. Patients in both groups also received best supportive care, as determined by their physician. The primary endpoint of the trial was overall survival (OS). Median OS in the ramucirumab group was 5.2 months, compared to 3.8 months in the placebo group. This difference was considered statistically significant. Hypertension was reported more frequently in the ramucirumab group than the placebo group.

Ramucirumab is designated as an orphan drug. The FDA accepted the BLA filing and granted priority review status to the application. A response to the BLA is expected in the second quarter of 2014.

Vedolizumab
Takeda has developed vedolizumab for the treatment of moderately to severely active Crohn’s disease (CD) or ulcerative colitis (UC). Vedolizumab is a monoclonal antibody directed against α4β7 integrin, which is found on certain white blood cells that have been shown to play a role in the inflammatory response.

The phase III program consisted of four trials to evaluate the efficacy of vedolizumab on clinical response and remission (along with effect on mucosal healing in UC), and long-term safety in patients with CD and UC who had failed at least one conventional therapy or a tumor necrosis factor (TNF) alpha inhibitor. Three of the trials were placebo-controlled, while one was an open-label trial. In all of the trials, 300 mg of vedolizumab was administered as an IV infusion at weeks zero, two and six and then every four or eight weeks thereafter.
Two separate BLAs were filed, one for CD and one for UC, in June 2013. The FDA granted priority review status to the application for UC and standard review to the application for CD.

**ABT-450, ABT-267, ABT-333**

AbbVie has developed three investigational direct-acting antiviral agents to be used for the treatment of chronic hepatitis C virus (HCV). This all-oral 3D regimen includes a boosted protease inhibitor (ABT-450 plus ritonavir*), an NS5A inhibitor (ABT-267) and a non-nucleoside polymerase inhibitor (ABT-333) in combination with ribavirin.*

The phase III program for this treatment regimen includes six trials in patients with genotype 1 HCV. The results of the first trial, SAPPHIRE-I, were recently reported. In this randomized, double-blind, placebo-controlled trial, 631 treatment-naïve genotype 1 HCV patients with no liver cirrhosis were enrolled and assigned to the 3D regimen plus ribavirin for 12 weeks (473 patients) or placebo for the first 12 weeks (158 patients). Patients who were initially assigned to the placebo group then received open-label treatment with the 3D regimen plus ribavirin for 12 weeks. The regimen is administered as a fixed-dose combination of ABT-450/ritonavir (150 mg/100 mg) coformulated with ABT-267 (25 mg) dose once daily in combination with ABT-333 (250 mg) and ribavirin (weight-based), both dosed twice daily.

The primary endpoint of SAPPHIRE-I was the percentage of subjects with sustained virologic response 12 weeks (SVR12) post treatment. After 12 weeks of active treatment, 96 percent (455 of 473) of patients achieved an SVR12. The most common adverse events reported were fatigue, headache and nausea. AbbVie expects the results from the other five trials in the coming months, and is planning regulatory submissions for approval of the 3D regimen in the second quarter of 2014. The FDA has designated the 3D regimen as a breakthrough therapy.
### Medications recently approved

<table>
<thead>
<tr>
<th>Manufacturer/Drug name</th>
<th>Indication</th>
<th>Mechanism of action/Drug class</th>
<th>Route of administration</th>
<th>Approval date</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Bleeding disorders</strong></td>
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<tr>
<td>Novo Nordisk/Novoeight (turoctocog alfa)</td>
<td>For use in adults and children with hemophilia A for control and prevention of bleeding episodes, for perioperative management and for routine prophylaxis to prevent or reduce the frequency of bleeding episodes</td>
<td>Replaces deficient factor/Factor replacement therapy</td>
<td>IV infusion</td>
<td>10/15/13</td>
<td>• Launch planned for shortly after April 2015</td>
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<tr>
<td><strong>Hepatitis</strong></td>
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<tr>
<td>Gilead Sciences/Sovaldi (sofosbuvir)</td>
<td>For the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen</td>
<td>Prevents virus replication/Nucleotide analog NS5B polymerase inhibitor</td>
<td>Oral</td>
<td>12/6/13</td>
<td>• First all-oral treatment regimen approved for genotypes 2 and 3</td>
</tr>
<tr>
<td>Janssen and Medivir AB/Olysio (simeprevir)</td>
<td>For the treatment of CHC infection as a component of a combination antiviral treatment regimen</td>
<td>Prevents virus replication/NS3/4A protease inhibitor</td>
<td>Oral</td>
<td>11/22/13</td>
<td>• First once-daily protease inhibitor approved for the treatment of CHC</td>
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<td><strong>Inflammatory diseases</strong></td>
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<tr>
<td>Genentech/Actemra* (tocilizumab)</td>
<td>For the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs)</td>
<td>Blocks Interleukin (IL)-6 receptors/Monoclonal antibody</td>
<td>Subcutaneous (SC) injection</td>
<td>10/21/13</td>
<td>• Previously approved as an IV infusion for the treatment of RA, polyarticular juvenile idiopathic arthritis (PJIA) and systemic juvenile idiopathic arthritis (SJIA)</td>
</tr>
<tr>
<td>Janssen/Stelara (ustekinumab)</td>
<td>For the treatment of adult patients with active psoriatic arthritis (PsA)</td>
<td>Targets IL-12 and IL-23/Dual IL inhibitor</td>
<td>SC injection</td>
<td>9/20/13</td>
<td>• Previously approved for the treatment of psoriasis</td>
</tr>
<tr>
<td>UCB Pharma/Cimzia* (certolizumab pegol)</td>
<td>For the treatment of adult patients with active PsA and for the treatment of adults with active ankylosing spondylitis (AS)</td>
<td>Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor</td>
<td>SC injection</td>
<td>PsA 9/27/13 AS 10/17/13</td>
<td>• Previously approved for the treatment of CD and RA</td>
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### Pipeline medications in phase III trials

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<tr>
<td>Bayer HealthCare and Onyx Pharmaceuticals/Nexavar (sorafenib)</td>
<td>For the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma that is refractory to radioactive iodine treatment</td>
<td>Inhibits cell growth and survival/ Tyrosine kinase inhibitor (TKI)</td>
<td>Oral</td>
<td>11/22/13</td>
<td>• Previously approved for the treatment of hepatocellular carcinoma (HCC) and renal cell carcinoma (RCC)</td>
</tr>
<tr>
<td>Genentech/Gazyva* (obinutuzumab)</td>
<td>In combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)</td>
<td>Targets the CD20 protein on malignant B-cells/ Anti-CD20 antibody</td>
<td>IV infusion</td>
<td>11/1/13</td>
<td>• First product approved with the FDA’s breakthrough therapy designation</td>
</tr>
<tr>
<td>Pharmacycics/Imbruvica (ibrutinib)</td>
<td>For the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy</td>
<td>Inhibits cell growth and survival/ Bruton’s tyrosine kinase (BTK) inhibitor</td>
<td>Oral</td>
<td>11/13/13</td>
<td>• First BTK inhibitor approved</td>
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<tr>
<td>Roche/Perjeta* (pertuzumab)</td>
<td>In combination with Herceptin* (trastuzumab) and docetaxel* for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory or early stage breast cancer</td>
<td>Prevents the HER2 receptor from pairing with other HER receptors/ HER2 receptor antagonist</td>
<td>IV infusion</td>
<td>9/30/13</td>
<td>• Previously approved for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease</td>
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<td><strong>Pulmonary hypertension</strong></td>
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<td>Actelion/Opsumit* (macitentan)</td>
<td>For the treatment of pulmonary arterial hypertension (PAH, WHO Group 1)</td>
<td>Reduces vascular smooth muscle constriction/ Endothelin receptor antagonist</td>
<td>Oral</td>
<td>10/18/13</td>
<td>• Walgreens Specialty Pharmacy is a distributor of this medication</td>
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<tr>
<td>Bayer HealthCare/Adempas* (riociguat)</td>
<td>For the treatment of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH, WHO Group 4) after surgical treatment or inoperable CTEPH and for the treatment of PAH, WHO Group 1</td>
<td>Reduces vascular smooth muscle constriction/Soluble guanylate cyclase stimulator</td>
<td>Oral</td>
<td>10/8/13</td>
<td>• First product approved for CTEPH indication</td>
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<td><strong>Peyronie’s disease</strong></td>
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<td>Auxilium Pharmaceuticals/Xiaflex* (collagenase clostridium histolyticum)</td>
<td>For the treatment of adult men with Peyronie’s disease (PD) with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy</td>
<td>Breaks down collagen deposits/ Purified collagenase</td>
<td>Injection</td>
<td>12/6/13</td>
<td>• First product approved as an effective treatment for PD</td>
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| Baxter/BAX 855          | For the treatment and prevention of bleeding in patients with hemophilia A | Replaces deficient factor/Factor replacement therapy | IV infusion | • Completed enrollment of phase III trial November 2013  
• Regulatory filings planned for late 2014 |
| Biogen Idec/Alprolix (recombinant factor IX Fc fusion protein) | For the treatment and prevention of bleeding in patients with hemophilia B | Replaces deficient factor/Factor replacement therapy | IV infusion | • BLA filed January 2013  
• A response to the BLA was expected January 2014; however, the FDA has extended the review period  
• A response is now expected April 2014 |
| Biogen Idec/Eloctate (recombinant factor VIII Fc fusion protein) | For the treatment and prevention of bleeding in patients with hemophilia A | Replaces deficient factor/Factor replacement therapy | IV infusion | • BLA filed March 2013  
• FDA requested additional information related to the manufacturing process in November 2013 |
| **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 | • FDA granted breakthrough therapy designation  
• Data from two phase III trials expected in 2014, followed by new drug application (NDA) submission |
| **Duchenne muscular dystrophy** |            |                                |                         |          |
| Sarepta Therapeutics/ Eteplirsen | For the treatment of Duchenne muscular dystrophy (DMD) | Restores protein translation and dystrophin production/RNA modulator | IV infusion | • Designated as an orphan drug with fast-track status  
• NDA filing was planned for the first half of 2014; however, the FDA has indicated that a confirmatory trial should be conducted before filing for approval |
| **Endocrine disorders**  |            |                                |                         |          |
| NPS Pharmaceuticals/ Natpara (recombinant human parathyroid hormone) | For the treatment of hypoparathyroidism | Replaces deficient hormone/Hormone replacement therapy | SC injection | • BLA filed October 2013 |
| **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 | SC injection | • FDA accepted NDA for standard review September 2013 |
### Pipeline medications in phase III trials (continued)

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| AbbVie/ABT-450 + ritonavir, ABT-267, ABT-333 | In combination with ribavirin for the treatment of chronic 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  
• Results of first phase III trial reported November 2013  
• Regulatory submissions planned for the second quarter of 2014 |
| Gilead Sciences/Ledipasvir | In fixed-dose combination with sofosbuvir with or without ribavirin for the treatment of chronic HCV infection in genotype 1 patients | Prevents virus replication/NS5A inhibitor | Oral | • Three phase III trials ongoing  
• Regulatory submissions planned for the second quarter of 2014 |
| Hereditary angioedema   |            |                                |                         |          |
| Pharming Group NV and Santarus/Ruconest (C1 inhibitor) | For the treatment of acute attacks in patients with hereditary angioedema | Replaces deficient C1 inhibitor/C1 inhibitor replacement therapy | IV infusion | • Designated as an orphan drug  
• BLA filed April 2013  
• A response to the BLA is expected April 2014 |
| 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 a complete response letter April 2013  
• Gilead is addressing the FDA’s concerns with the NDA |
| Gilead Sciences/Elvitegravir | For the treatment of HIV in treatment-experienced patients | Prevents virus replication/Integrase inhibitor | Oral | • NDA filed June 2012  
• Received a complete response letter April 2013  
• Gilead is addressing the FDA’s concerns with the NDA |
### Pipeline medications in phase III trials (continued)

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<td><strong>Inflammatory diseases</strong></td>
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</table>
| Celgene/ Apremilast | For the treatment of PsA and psoriasis | Modulates the inflammatory response/Phosphodiesterase type 4 inhibitor | Oral | • NDA filed for PsA March 2013  
• NDA filing for psoriasis is expected in the fourth quarter of 2013 |
| Novartis/ Secukinumab (AIN457) | For the treatment of plaque psoriasis | Interferes with the inflammatory response/IL-17A inhibitor | SC injection | • Primary endpoint achieved in phase III trial July 2013  
• Regulatory filings expected in the fourth quarter of 2013 |
| Sanofi and Regeneron Pharmaceuticals/ Sarilumab | For the treatment of RA | Interferes with the inflammatory response/IL-16 inhibitor | SC injection | • Co-primary endpoints achieved in phase III trial November 2013  
• Four other phase III trials ongoing |
| Takeda/ Vedolizumab | For the treatment of moderately to severely active CD and UC | Modulates the inflammatory response/α4β7 integrin inhibitor | IV infusion | • BLA filed June 2013  
• FDA granted priority review status to UC application and standard review to CD application |
| **Lambert-Eaton Myasthenic Syndrome** | | | | |
| Catalyst Pharmaceutical Partners/ Firdapse (amifampridine phosphate) | For the treatment of 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 III results expected in the second quarter of 2014 |
| **Lipodystrophy** | | | | |
| Bristol-Myers Squibb and AstraZeneca/ Metreleptin | For the treatment of metabolic disorders associated with inherited or acquired lipodystrophy | Reduces fat accumulation in organs/Leptin analogue | SC injection | • Designated as an orphan drug  
• BLA accepted and granted priority review June 2013  
• A response to the BLA is expected February 2014 |
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<td><strong>Lysosomal storage diseases</strong></td>
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| 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 not achieved in stage I of first phase III trial December 2012  
• Stage II results are expected in the fourth quarter of 2013 |
| BioMarin Pharmaceutical/Vimizim (GALNS) | For the treatment of MPS IVA (Morquio A syndrome) | Replaces deficient N-acetylgalactosamine-6-sulfatase (GALNS)/Enzyme replacement therapy | IV infusion | • Designated as an orphan drug  
• BLA filed April 2013  
• FDA granted priority review status  
• A response to the BLA is expected February 2014 |
| Genzyme/Cerdelga (eliglustat) | For the treatment of Gaucher’s disease | Reduces the production of glucocerebroside/Glucosylceramide synthase inhibitor | Oral | • Designated as an orphan drug  
• NDA accepted and granted priority review June 2013 |
| 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 | • FDA granted breakthrough therapy designation for early onset LAL deficiency  
• Designated as an orphan drug with fast-track status  
• Enrollment in the phase III trial for late onset LAL deficiency completed December 2014 |
| **Multiple sclerosis** | | | | |
| Biogen Idec/Plegridy (peginterferon beta-1a) | For the treatment of relapsing-remitting multiple sclerosis (MS) | Unknown mechanism of action in MS/Interferon | SC injection | • Dosed once every two or four weeks  
• FDA granted fast-track status  
• BLA filed May 2013 |
| Teva Pharmaceuticals/Laquanimod | For the treatment of relapsing-remitting MS | Inhibits autoimmune and inflammatory disease activity/Immunomodulatory agent | Oral | • Third phase III trial is ongoing  
• This trial is being conducted under a special protocol assessment |
| **Neurogenic disorders** | | | | |
| Chelsea Therapeutics/Northera (droxidopa) | For the treatment of symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, dopamine beta-hydroxylase deficiency and nondiabetic autonomic neuropathy | Increases norepinephrine levels in the nervous system/Synthetic catecholamine | Oral | • Designated as an orphan drug with fast-track status  
• Received a complete response letter March 2012  
• FDA accepted resubmission of NDA  
• A response to the NDA is expected February 2014 |
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<td><strong>Neutropenia</strong></td>
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</table>
| Teva Pharmaceuticals/ Balugrastim | To reduce the duration of severe neutropenia in cancer patients undergoing chemotherapy | Long-acting granulocyte colony-stimulating factor | SC injection | • BLA filed December 2012  
• BLA withdrawn after discussions with the FDA November 2013 |
| Cell Therapeutics/ 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  
• Phase III trial ongoing |
| Eisai/Lenvatinib | For the treatment of thyroid cancer | Inhibits cell growth and survival | Oral | • Designated as an orphan drug |
| Eli Lilly/ Necitumumab | For the treatment of non-small cell lung cancer (NSCLC) | Reduces tumor cell growth and blood supply/Epidermal growth factor receptor inhibitor | IV infusion | • Primary endpoint achieved in phase III trial  
• Filing anticipated by the end of 2014 |
| Eli Lilly/ Ramucirumab | For the second-line treatment of gastric cancer | Reduces tumor cell growth and blood supply/VEGF receptor inhibitor | IV infusion | • Designated as an orphan drug  
• BLA filed in the fourth quarter of 2013  
• FDA granted priority review status  
• A response to the BLA is expected in the second quarter of 2014 |
| **Oncology**              |            |                                |                         |          |
| Gilead Sciences/ Idelalisib | For the treatment of indolent non-Hodgkin's lymphoma (iNHL) and in combination with Rituxan (rituximab) for the treatment of relapsed CLL | Inhibits cell growth and survival/ Phosphoinositide 3-kinase inhibitor | Oral | • FDA granted breakthrough therapy designation for CLL indication  
• NDA for iNHL filed September 2013 |
| Janssen/ Siltuximab | For the treatment of multicentric Castleman disease in patients who are HIV-negative and human herpes virus 8-negative | Interferes with the inflammatory response/ IL-6 inhibitor | IV infusion | • Designated as an orphan drug  
• BLA filed September 2013  
• FDA granted priority review status |
| Novartis/ LDK378 | For the treatment of anaplastic lymphoma kinase positive (ALK+) NSCLC in patients previously treated with Xalkori (crizotinib) | Inhibits cell growth and survival/ALK inhibitor | Oral | • FDA granted breakthrough therapy designation  
• NDA filing planned for 2014 |
| Novartis/ Panobinostat | For the treatment of relapsed or refractory multiple myeloma (MM) | Inhibits cell growth and survival/Histone deacetylase inhibitor | Oral | • Primary endpoint achieved in phase III trial December 2013  
• Regulatory filings planned for 2014 |
Pipeline medications in phase III trials (continued)

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| Onconova Therapeutics/ Rigosertib | For the treatment of refractory myelodysplastic syndromes (MDS) | Targets alpha and beta isoforms of PI-3 kinases/Multikinase inhibitor | IV infusion | • An oral formulation is also in development  
• Phase III data expected at the end of 2013 or early 2014 |
| Pfizer/ Palbociclib      | For the treatment of breast cancer | Prevents tumor cell progression/ Cyclin-dependent kinase inhibitor | Oral | • FDA granted breakthrough therapy designation  
• Phase III trials ongoing |
| Sanofi/ Fedratinib (SAR302503) | For the treatment of myelofibrosis (MF) | Inhibits the formation and development of blood cells/Janus-associated kinase inhibitor | Oral | • Primary endpoint achieved in phase III trial May 2013  
• Sanofi cancelled development plans after determining that the safety risks of fedratinib outweigh the potential benefits to patients |
| Spectrum Pharmaceuticals/ Belinostat | For the treatment of relapsed or refractory peripheral T-cell lymphoma | Inhibits cell growth and survival/Histone deacetylase inhibitor | IV infusion | • Designated as an orphan drug  
• NDA filed December 2013 |
| **Pulmonary hypertension** |            |                                |                         |          |
| Actelion/ Selexipag      | For the treatment of PAH | Reduces vascular smooth muscle constriction/ Prostacyclin receptor agonist | Oral | • Results from phase III trial expected in mid-2014 |
# New dosage forms in the pipeline

<table>
<thead>
<tr>
<th>Manufacturer/Drug name</th>
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<th>Mechanism of action/Drug class</th>
<th>Current route of administration</th>
<th>Investigational route of administration*</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Multiple sclerosis</strong></td>
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| 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 | SC injection | • Phase III results expected in 2014  
• Previously marketed as Zenapax* for the prevention of acute kidney rejection |
| Teva Pharmaceuticals/Copaxone (glatiramer acetate) | For the treatment of relapsing-remitting MS | Modulates the immune system/Disease-modifying therapy | SC injection | SC injection | • Higher dose formulation administered three times a week instead of daily  
• Supplemental new drug application (sNDA) accepted May 2013 |
| **Neuroendocrine disorders** |            |                                |                                 |                                          |          |
| Novartis/Signifor LAR (pasireotide long-acting release) | For the treatment of acromegaly | Binds somatostatin receptors/Somatostatin analogue | SC injection | Intramuscular (IM) injection | • Monthly IM injection  
• Primary endpoint achieved in phase III trial July 2013 |
| **Oncology** |            |                                |                                 |                                          |          |
| Roche/Herceptin (trastuzumab) | For the treatment of HER2-positive early breast cancer | Inhibits the proliferation of tumor cells that overexpress HER2/Monoclonal antibody | IV infusion | SC injection | • Coprimary endpoints achieved in phase III trial October 2011  
• Additional studies are currently ongoing |
| **Pulmonary hypertension** |            |                                |                                 |                                          |          |
| United Therapeutics/Treprostinil diolamine | For the treatment of PAH | Dilates pulmonary blood vessels/Prostacyclin analogue | Continuous SC or IV infusion and inhalation | Oral | • Received first complete response letter October 2012  
• Received second complete response letter March 2013  
• FDA accepted resubmission of NDA  
• A response to the NDA is expected February 2014 |

*Dosage form is not available. Only investigational route of administration is available at this time.
## New indications in the pipeline

<table>
<thead>
<tr>
<th>Manufacturer/ Drug name</th>
<th>Current indication</th>
<th>Investigational indication</th>
<th>Mechanism of action/Drug class</th>
<th>Route of administration</th>
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<td><strong>Bleeding disorders</strong></td>
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<td>Baxter/Feiba NF* (anti-inhibitor coagulant complex)</td>
<td>For the treatment of bleeding episodes or to cover surgical interventions in patients with hemophilia A or B with inhibitors</td>
<td>For the prevention of bleeding in patients with hemophilia A or B and inhibitors</td>
<td>Replaces deficient factor/ Factor replacement therapy</td>
<td>IV infusion</td>
<td>• Supplemental biologics license application (sBLA) filed February 2013</td>
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<td><strong>Cystic fibrosis</strong></td>
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| Vertex Pharmaceuticals/ Kalydeco (ivacaftor) | For the treatment of CF in patients ages 6 and older who have a G551D mutation in the CFTR gene | For the treatment of CF in patients ages 6 and older who have at least one non-G551D CFTR gating mutation | Increases chloride ion transport across cell membranes/ CFTR potentiator | Oral | • Designated as an orphan drug  
• sNDA filed September 2013 |
| **Inflammatory diseases** |                    |                             |                                |                         |          |
| AbbVie/Humira* (adalimumab) | For the treatment of RA, PJIA, PsA, AS, CD, UC and psoriasis | For the treatment of hidradenitis suppurativa | Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor | SC injection | • Results from phase III trials are expected in 2014 |
| Novartis/Xolair* (omalizumab) | For the treatment of allergic asthma | For the treatment of chronic idiopathic urticaria | Inhibits the binding of immunoglobulin E (IgE)/IgE-directed antibody | SC injection | • sBLA filing accepted October 2013  
• A response to the sBLA is expected in the second quarter of 2014 |
| UCB Pharma/ Cimzia* (certolizumab pegol) | For the treatment of CD, RA, PsA and AS | For the treatment of axial spondyloarthritis | Targets TNF alpha, which is involved in the inflammatory process/TNF inhibitor | SC injection | • Received a complete response letter October 2013 |
| **Multiple sclerosis**  |                    |                             |                                |                         |          |
| Biogen Idec and Elan/Tysabri* (natalizumab) | For the treatment of relapsing forms of MS (generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy) and for the treatment of CD | For the first-line treatment of relapsing forms of MS in patients who have tested negative for antibodies to the JC virus | Binds and inhibits alpha-4 integrins from adhering to their counter-receptors/ Selective adhesion molecule inhibitors | IV infusion | • sBLA filed January 2013 |
### New indications in the pipeline (continued)

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| Genzyme/Lemtrada (alemtuzumab) | For the treatment of B-cell CLL | For the treatment of relapsing MS | Binds to the CD52 antigen on B-cells and T-cells/Therapeutic antibody | IV infusion | • FDA granted fast track status  
• sBLA filed June 2012  
• A response to the sBLA is expected December 2013  
• Marketed as Campath* for CLL indication |
| Celgene/Revlimid* (lenalidomide) | For the treatment of previously treated MM, MDS and relapsed of refractory MCL | For the treatment of newly diagnosed MM | Posesses immuno-modulatory, anti-inflammatory and antiangiogenic properties/Thalidomide analogue | Oral | • Primary endpoint achieved in phase III trial July 2013  
• sNDA filing planned for the first quarter of 2014 |
| GlaxoSmithKline/Mekinist (trametinib) | For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations | In combination with Tafinlar for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation | Inhibits cell growth and survival/Mitogen-activated extracellular signal regulated kinase inhibitor | Oral | • sNDA filed July 2013  
• FDA granted priority review  
• A response to the sNDA is expected January 2014 |
| GlaxoSmithKline/Tafinlar (dabrafenib) | For the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation | In combination with Mekinist for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation | Inhibits cell growth and survival/BRAF kinase inhibitor | Oral | • sNDA filed July 2013  
• FDA granted priority review  
• A response to the sNDA is expected January 2014 |
| GlaxoSmithKline/Votrient* (pazopanib) | For the treatment of RCC and soft tissue sarcoma | For the treatment of advanced epithelial ovarian cancer | Inhibits cell growth and survival/TKI | Oral | • Designated as an orphan drug  
• Primary endpoint achieved in phase III trial June 2013 |
| GlaxoSmithKline and Genmab/Arzerra* (ofatumumab) | For the treatment of patients with CLL refractory to fludarabine* and alemtuzumab* | In combination with an alkylator-based therapy for the treatment of CLL in patients who are treatment-naive or ineligible for fludarabine-based therapy | Targets the CD20 protein on malignant B-cells/Anti-CD20 antibody | IV infusion | • FDA granted breakthrough therapy designation  
• sBLA filed October 2013 |
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| 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 | Inhibits the formation and development of blood cells/Janus kinase (JAK) inhibitor | Oral | • FDA granted fast-track status  
• Phase III results expected in early 2014  
• sNDA filing planned for the first half of 2014 |
| Pharmacyscics/Imbruvica (ibrutinib) | For the treatment of patients with MCL who have received at least one prior therapy | For the treatment of CLL/small lymphocytic lymphoma (SLL) and Waldenstrom’s macroglobulinemia | Inhibits cell growth and survival/BTK inhibitor | Oral | • Designated as an orphan drug  
• FDA granted breakthrough therapy designation  
• NDA filed for CLL/SLL July 2013  
• FDA granted priority review status |
| **Ophthalmology**       |                   |                             |                                |                         |          |
| Regeneron Pharmaceuticals/Eylea (aflibercept) | For the treatment of neovascular (wet) age-related macular degeneration and macular edema following central retinal vein occlusion | For the treatment of diabetic macular edema | Binds vascular endothelial growth factor and placental growth factor/Anti-angiogenesis inhibitor | Intravitreal injection | • Primary endpoint achieved in two phase III trials August 2013  
• sBLA filed in the fourth quarter of 2013 |
Glossary of terms

Antibody-drug conjugate—consists of a monoclonal antibody linked to a cytotoxic drug.

BLA—stands for “biologics license application,” similar to an NDA but used for investigational medications that are considered to be biologic agents.

Boxed warning—designated for prescriptions that pose a significant risk of serious or life-threatening adverse effects based on medical studies.

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 III 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 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.

Refusal to file letter—a letter the FDA issues to the applicant if it determines the application is not sufficiently complete.

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.

SPA—stands for “special protocol assessment,” an agreement with the FDA that the manufacturer’s clinical protocol for a phase III trial is acceptable to support an NDA or BLA.

Treatment-naive—patients who have never been treated before for a particular condition.
References

Journals:


Websites:
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ClinicalTrials.gov—clinicaltrials.gov
Manufacturers’ websites
U.S. Food and Drug Administration—fda.gov

Information in the report is current as of December 2013, and was accessed on December 11, 2013.
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