Biopharmaceutical Research Companies Receive Approval for 35 New Treatments in 2011

America’s biopharmaceutical research companies obtained approval for 35 new medicines in 2011 from the U.S. Food and Drug Administration (FDA). The medicines include 24 new drugs (also called new molecular entities or NMEs), six therapeutic biologics, and five other biologics. Eleven of the new medicines are orphan drugs. Among the new medicines:

- Eight new medicines for the treatment of cancer, including the first approved treatment for advanced medullary cancer, the first in a new class of drugs for two types of lymphoma, and a personalized medicine for non-small-cell lung cancer.
- Six medicines for infectious diseases, including the first antibacterial approved for *Clostridium difficile*-associated diarrhea in nearly 30 years and two new hepatitis C treatments.
- Three new medicines for cardiovascular disease, including one for acute coronary syndrome and one for the prevention of deep vein thrombosis.
- Three new medicines for genetic disorders, including the first treatment for factor XIII deficiency, a rare bleeding disorder, and the first treatment for hereditary angioedema in adults.
- Three medicines were approved for neurological disorders, including one for a severe form of childhood epilepsy, Lennox-Gastaut syndrome.
- Two imaging agents were approved, including the first for differentiating between Parkinson’s disease and essential tremor.
- Two new medicines were approved for chronic obstructive pulmonary disease (COPD), including the first in a new class of drugs for the disease.
- A recombinant fusion protein for the treatment of age-related macular degeneration.
- The first new medicine in more than 50 years for the treatment of systemic lupus erythematosus.
- A new medicine for the treatment of major depressive disorder.
- The first and only personalized aesthetic cell therapy for the improvement of smile lines.
- A new medicine for the prevention of rejection of kidney transplantation.
- The first specific treatment for scorpion stings.
- A new albumin approved for diseases benefitting from albumin therapy, such as hypovolemic shock and adult respiratory distress syndrome.

approved medicines by therapeutic category, 2011

- Cancer: 8
- Genetic Disorders: 3
- Heart Disease: 3
- Infectious Diseases: 6
- Neurological Disorders: 3
- Other: 12

continued on page 2
New Drug and Therapeutic Biological Approvals in 2011

Pharmaceutical Research Companies Receive Approval for 35 New Treatments in 2011

continued from page 1

Detailed descriptions of the new medicines approved in 2011 begin on page 9.

Overall, the FDA approved 102 new therapeutics—the 24 new molecular entities (NMEs), 11 biologics, and 67 additional new medicines.

Drug development remains an expensive and lengthy process. The average research and development cost of an approved medicine is $1.2 billion, including the cost of failures, according to a 2007 report from the Tufts Center for the Study of Drug Development.

In 2011, PhRMA members alone invested an estimated $49.5 billion in discovering and developing new medicines. (See page 17 for more information on R&D and sales.) In addition, according to Tufts, it now takes an average of 10 to 15 years to bring a new medicine from the laboratory to the pharmacy. The FDA’s review of a company’s application consumes a portion of that time.

In 2011, the 30 new therapeutics approved by FDA’s Center for Drug Evaluation and Research (CDER) were reviewed in an average of 15.0 months.

The new medicines approved last year join the impressive medicine chest that America’s research-based biopharmaceutical companies have developed to help patients. The medicines in the pharmaceutical industry pipeline promise millions of patients new hope for an even healthier tomorrow.

As in past years, there are an increasing number of potential new drugs entering clinical testing. According to the Adis R&D Insight database, today there are more than 3,000 medicines in development in the United States. In 2005, there were 2,400 medicines in development. These new medicines hold the promise of better prevention, treatments, and cures for a broad range of diseases and conditions.

In addition to developing new treatments, in 2005 PhRMA member companies helped form the “Partnership for Prescription Assistance” (PPA) to help patients without access to prescription drug coverage receive the medicines they need from the program that’s right for them. Since April 2005, PPA has connected more than 7 million patients to one or more national, state, and industry-sponsored patient assistance programs that provide eligible patients their medicines for free or nearly free.

The new medicines approved last year join the impressive medicine chest that America’s research-based biopharmaceutical companies have developed to help patients. The medicines in the pharmaceutical industry pipeline promise millions of patients new hope for an even healthier tomorrow.
## New Drug and Therapeutic Biological Approvals in 2011*

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</tr>
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<tbody>
<tr>
<td>Adcetris™ brentuximab vedotin (P) (Orphan Drug)</td>
<td>Seattle Genetics Bothell, WA</td>
<td>Hodgkin lymphoma, systemic anaplastic large-cell lymphoma</td>
<td>2/28/11</td>
<td>8/19/11</td>
<td>5.7 months</td>
</tr>
</tbody>
</table>

For more information, contact: Seattle Genetics at (425) 527-4000 or www.adcetris.com

| Arclapta™ Neohaler™ indacaterol inhalation powder (S) | Novartis Pharmaceuticals East Hanover, NJ | chronic obstructive pulmonary disease (COPD) | 12/18/2008 | 7/1/2011 | 30.4 months |

For more information, contact: Novartis Pharmaceuticals at (888) 669-6681 or www.arclapta.com


For more information, contact: GlaxoSmithKline at (888) 825-5249, Human Genome Sciences at (301) 309-8504 or www.benlysta.com

| Brilinta™ ticagrelor tablets (S) | AstraZeneca Wilmington, DE | acute coronary syndrome | 11/16/2009 | 7/20/2011 | 20.1 months |

For more information, contact: AstraZeneca at (800) 236-9933 or www.brilinta.com

| Caprelsa® vandetanib tablets (P) (Orphan Drug) | AstraZeneca Wilmington, DE | medullary thyroid cancer | 7/7/2010 | 4/6/2011 | 9.0 months |

For more information, contact: AstraZeneca at (800) 236-9933 or www.caprelsa.com

| Daliresp® roflumilast tablets (S) | Forest Laboratories New York, NY | COPD | 7/17/2009 | 2/28/2011 | 19.5 months |

For more information, contact: Forest Laboratories at (800) 678-1605 or www.daliresp.com

| DaTscan™ ioflupane I-123 injection (P) | GE Healthcare Waukesha, WI | detection of Parkinson's disease using SPECT imaging | 3/9/2009 | 1/14/2011 | 22.3 months |

For more information, contact: GE Healthcare at www.us.datscan.com

*Approved by the Center for Drug Evaluation and Review (CDER).
(S) – Standard Review
(P) – Priority Review
† Original submission was made on 12/18/2008; a complete response to previous action was submitted on 10/1/2010; review time is calculated from 12/18/2008.
†† Original submission was made on 11/16/2009; a complete response to previous action was submitted on 1/20/2011; review time is calculated from 11/16/2009.
††† Original submission was made on 7/17/2009; a complete response to previous action was submitted on 8/30/2010; review time is calculated from 7/17/2009.
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<td><strong>Dificid®</strong></td>
<td>Optimer Pharmaceuticals San Diego, CA</td>
<td><em>Clostridium difficile</em>-associated diarrhea</td>
<td>11/30/2010</td>
<td>5/27/2011</td>
<td>5.9 months</td>
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<tr>
<td>fidaxomicin tablets (P)</td>
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<tr>
<td><strong>Edarbi™</strong></td>
<td>Takeda Pharmaceuticals North America Deerfield, IL</td>
<td>hypertension</td>
<td>4/27/2010</td>
<td>2/25/2011</td>
<td>10.0 months</td>
</tr>
<tr>
<td>azilsartan medocomi (S)</td>
<td></td>
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<td>rilpivirine tablets (S)</td>
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<tr>
<td><strong>Erwinaze™</strong></td>
<td>EUSA Pharma Langhome, PA</td>
<td>acute lymphoblastic leukemia (ALL)</td>
<td>11/1/2010</td>
<td>11/18/2011</td>
<td>12.6 months</td>
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<tr>
<td>asparaginase Erwinia chrysanthemi (S) (Orphan Drug)</td>
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<tr>
<td><strong>Eylea®</strong></td>
<td>Regeneron Pharmaceuticals Tarrytown, NY</td>
<td>wet (neovascular) age-related macular degeneration (AMD)</td>
<td>2/18/2011</td>
<td>11/18/2011</td>
<td>9.0 months</td>
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<td>aflibercept injection (P)</td>
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<tr>
<td><strong>Ferriprox®</strong></td>
<td>ApoPharma Toronto, Canada</td>
<td>iron overload due to blood transfusions in patients with thalassemia</td>
<td>1/30/2009</td>
<td>10/14/2011</td>
<td>32.5 months</td>
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<td>deferiprone (S) (Orphan Drug)</td>
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<tr>
<td><strong>Firazyr®</strong></td>
<td>Shire Human Genetic Therapies Cambridge, MA</td>
<td>acute attacks of hereditary angioedema</td>
<td>10/28/2007</td>
<td>8/25/2011</td>
<td>46.0 months</td>
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<tr>
<td>icatibant injection (P) (Orphan Drug)</td>
<td></td>
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</table>

For more information, contact:

Optimer Pharmaceuticals at (858) 909-0736 or www.dificid.com

Takeda Pharmaceuticals North America at (877) 825-3327 or www.edarbi.com

Janssen Therapeutics at (800) 526-7736 or www.edurant-info.com

EUSA Pharma at (800) 833-8533 or www.erwinaze.com

Regeneron Pharmaceuticals at (877) 734-6777 or www.eylea.com

ApoPharma at (800) 268-4623 or www.ferriprox.com

Shire Human Genetic Therapies at (866) 888-0660 or www.firazyr.com

† Original submission was made on 1/30/2009; a complete response to previous action was submitted on 4/14/2011; review time is calculated from 1/30/2009.

†† Original submission was made on 10/26/2007; a complete response to previous action was submitted on 2/25/2011; review time is calculated from 10/26/2007.
### New Drug and Therapeutic Biological Approvals in 2011

<table>
<thead>
<tr>
<th>Product</th>
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<th>FDA Approved</th>
<th>Review Time</th>
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<tbody>
<tr>
<td>Gadavist™</td>
<td>Bayer HealthCare Pharmaceuticals Wayne, NJ</td>
<td>imaging agent for central nervous system (CNS) scans</td>
<td>5/14/2010</td>
<td>3/14/2011</td>
<td>10.0 months</td>
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<tr>
<td>Jakafi™</td>
<td>Incyte Wilmington, DE</td>
<td>myelofibrosis</td>
<td>6/3/2011</td>
<td>11/16/2011</td>
<td>5.5 months</td>
</tr>
<tr>
<td>Natroba™</td>
<td>ParaPRO Carmel, IN</td>
<td>head lice infestation</td>
<td>1/22/2009</td>
<td>1/18/2011</td>
<td>23.9 months</td>
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<tr>
<td>Onfi™</td>
<td>Lundbeck Deerfield, IL</td>
<td>Lennox-Gastaut syndrome</td>
<td>12/23/2010</td>
<td>10/21/2011</td>
<td>10.0 months</td>
</tr>
</tbody>
</table>

*For more information, contact: Bayer HealthCare Pharmaceuticals at (888) 842-2937 or www.gadavist.com

*For more information, contact: GlaxoSmithKline at (888) 825-5249, XenoPort at (408) 616-7200 or www.horizant.com

*For more information, contact: Vertex Pharmaceuticals at (617) 444-6100 or www.incivek.com

*For more information, contact: Incyte at (855) 446-2983 or www.jakafi.com

*For more information, contact: ParaPRO at askus@parapro.com or www.natroba.com

*For more information, contact: Bristol-Myers Squibb at (800) 332-2056 or www.nulojix.com

*For more information, contact: Lundbeck at (866) 337-6996 or www.onfi.com

† Original submission was made on 7/1/2009; a complete response to previous action was submitted on 12/15/2010; review time is calculated from 7/1/2009.
**New Drug Approvals in 2011**

<table>
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<tbody>
<tr>
<td>Potiga™ ezogabine tablets (S)</td>
<td>GlaxoSmithKline Rsch. Triangle Park, NC Valeant Pharmaceuticals International Mississauga, Canada</td>
<td>partial-onset seizures associated with epilepsy</td>
<td>10/30/2009</td>
<td>6/10/2011</td>
<td>18.1 months</td>
</tr>
<tr>
<td>Tradjenta™ linagliptin tablets (S)</td>
<td>Boehringer Ingelheim Pharmaceuticals Ridgefield, CT</td>
<td>type 2 diabetes</td>
<td>7/2/2010</td>
<td>5/2/2011</td>
<td>10.0 months</td>
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<tr>
<td>Victrelis™ boceprevir (P)</td>
<td>Merck Whitehouse Station, NJ</td>
<td>chronic hepatitis C</td>
<td>11/15/2010</td>
<td>5/13/2011</td>
<td>5.9 months</td>
</tr>
<tr>
<td>Viibryd® vilazodone HCl (S)</td>
<td>Forest Laboratories New York, NY</td>
<td>major depressive disorder</td>
<td>3/22/2010</td>
<td>1/21/2011</td>
<td>10.0 months</td>
</tr>
<tr>
<td>Xarelto® rivaroxaban tablets (S)</td>
<td>Janssen Pharmaceuticals Titusville, NJ</td>
<td>blood clots, deep vein thrombosis, pulmonary embolism prevention following knee or hip replacement surgery</td>
<td>7/28/2008</td>
<td>7/1/2011</td>
<td>37.0 months</td>
</tr>
</tbody>
</table>

For more information, contact: GlaxoSmithKline at (888) 825-5249 or www.gsk.com

For more information, contact: Boehringer Ingelheim at (800) 243-0127 or www.tradjenta.com

For more information, contact: Merck at (800) 444-2080 or www.victrelis.com

For more information, contact: Forest Laboratories at (800) 678-1605 or www.viibryd.com

For more information, contact: Pfizer at (212) 733-2323 or www.xalkori.com

For more information, contact: Janssen Pharmaceuticals at (800) 775-5514 or www.xarelto.com

For more information, contact: Bristol-Myers Squibb at (800) 332-2056 or www.yervoy.com

† Original submission was made on 7/28/2008; a complete response to previous action was submitted on 1/3/2011; review time is calculated from 7/28/2008.
### New Biological Approvals in 2011*

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<tbody>
<tr>
<td>Anascorp&lt;sup&gt;®&lt;/sup&gt; centruroides (Scorpion) immune F(ab’)&lt;sub&gt;2&lt;/sub&gt; (equine) injection (P) (Orphan Drug)</td>
<td>Rare Disease Therapeutics Franklin, TN</td>
<td>treatment of scorpion stings</td>
<td>1/22/2009 2/1/2011&lt;sup&gt;†&lt;/sup&gt;</td>
<td>8/3/2011</td>
<td>29.4 months</td>
</tr>
<tr>
<td>Arдовax™ adenovirus type 4 and type 7 vaccine, live, oral (S)</td>
<td>Teva North America North Wales, PA</td>
<td>immunization for the prevention of febrile acute respiratory disease (ARD) in military population</td>
<td>9/14/2010&lt;sup&gt;††&lt;/sup&gt;</td>
<td>3/16/2011</td>
<td>29.5 months</td>
</tr>
<tr>
<td>Corifact&lt;sup&gt;®&lt;/sup&gt; factor XIII concentrate (human) (P) (Orphan Drug)</td>
<td>CSL Behring King of Prussia, PA</td>
<td>treatment of congenital factor XIII deficiency</td>
<td>8/18/2010</td>
<td>2/15/2011</td>
<td>6.0 months</td>
</tr>
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* Approved by the Center for Biologics Evaluation and Review.
(S) – Standard Review
(P) – Priority Review

† Original submission was made on 1/22/2009; a complete response to previous action was submitted on 2/1/2011; review time is calculated from 1/22/2009.

†† Original submission was made on 9/30/2008; a complete response to previous action was submitted on 9/14/2010; review time is calculated from 9/30/2008.

For more information, contact: Rare Disease Therapeutics at (615) 399-0700 or www.raretx.com

For more information, contact: Teva Pharmaceuticals USA at (888) 838-2872

For more information, contact: CSL Behring at (800) 504-5434 or www.corifact.com
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<tr>
<td>Kedbumin™ albumin (human), sterile, aqueous solution for single dose intravenous administration (S)</td>
<td>Kedrion Barga, Italy</td>
<td>hypovolemic shock, hypoalbuminemia, central volume depletion due to cirrhotic ascites, ovarian hyperstimulation syndrome, adult respiratory distress syndrome, burns, hemodialysis, use in cardiopulmonary bypass procedures</td>
<td>8/3/2010</td>
<td>6/3/2011</td>
<td>10.0 months</td>
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<tr>
<td>laViv™ azficel-T (S)</td>
<td>Fibrocell Science Exton, PA</td>
<td>improvement of nasolabial fold wrinkles in adults</td>
<td>12/22/2010</td>
<td>6/21/2011</td>
<td>6.0 months</td>
</tr>
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</table>

*For more information, contact: Kedrion at www.kedrion.com*

*For more information, contact: Fibrocell Science at (484) 713-6000 or www.mylaviv.com*

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The content of this survey has been obtained through government and industry sources. The information may not be comprehensive. For more specific information about a particular product, contact the individual company directly.

A publication of PhRMA’s Communications & Public Affairs Department. (202) 835-3460

www.phrma.org | www.innovation.org | www.pparx.org | www.buysafedrugs.info

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Pharmaceutical Research and Manufacturers of America • 950 F Street, NW, Washington, DC 20004
A Look at the New Drugs and Biologics Approved in 2011

Thirty-five new drugs and biologics developed by America’s biopharmaceutical research companies were approved by the U.S. Food and Drug Administration (FDA) for patients in 2011. These new medicines represent significant advancements in the treatment of a wide range of diseases, and will contribute to improved patient care, disease treatment and prevention as well as help patients to live longer and healthier lives.

**Autoimmune Diseases**

**Benlysta®** (belimumab) is the first new medicine approved to treat lupus in more than 50 years and the first in a new class of drugs called BlyS-specific inhibitors. It is indicated for the treatment of adults with active, autoantibody-positive systemic erythematosus lupus (SLE). It is delivered by intravenous fusion and is designed to target the B-lymphocyte stimulator (BlyS) protein, which may reduce the number of abnormal B cells thought to be a problem in SLE. In the United States, SLE affects between 300,000 to 1.5 million people, most of which are women.

Benlysta works by blocking the binding of BlyS to its receptors on B cells. It inhibits the survival of B cells, including the auto-reactive cells and reduces differentiation of B cells into immunoglobulin-producing plasma cells.

Benlysta was developed jointly by GlaxoSmithKline and Human Genome Sciences, Inc.

**Cancer**

Eight new medicines for the treatment of cancer were approved, including the first approved treatment for advanced medullary cancer, the first in a new class of drugs for two types of lymphoma, and a personalized medicine for non-small-cell lung cancer.

**Adcetris™** (brentuximab vedotin), the first in a new class of antibody-drug conjugates (ADCs), was approved to treat Hodgkin lymphoma and systemic anaplastic large cell lymphoma (ALCL), a rare type of lymphoma that represents only 3 percent of all non-Hodgkin lymphomas. ADCs combine a monoclonal antibody and a therapeutic drug, where the antibody directs the therapeutic to target the cancerous cells. It is also the first FDA-approved drug for Hodgkin lymphoma in more than 30 years and the first to specifically treat ALCL.

Adcetris is composed of an anti-CD30 monoclonal antibody and a microtubule disrupting agent and releases its therapeutic drug once inside the CD30-expressing tumor cells.

In clinical trials, 73 percent of Hodgkin lymphoma patients achieved either a complete or partial response to treatment for an average of 6.7 months, while 86 percent of patients with ALCL experienced either a complete or partial response for an average 12.6 months.

Adcetris was developed by Seattle Genetics, Inc.

**Caprelsa®** (vandetanib tablets) is the only FDA-approved treatment for advanced medullary thyroid cancer. It is indicated for the treatment of medullary thyroid cancer that cannot be removed by surgery or that has spread to other parts of the body. It is kinase inhibitor that targets the medullary thyroid cancer’s ability to grow and expand.

There are about 44,000 new cases of thyroid cancer each year, and about 2,000 people die from the disease. Medullary thyroid cancer makes up about 3 percent to 5 percent of all thyroid cancer cases—about 1,300 to 2,200 cases each year.

In clinical trials, patients treated with Caprelsa versus placebo were found to have a 65 percent reduction in risk for disease progression.

Caprelsa was developed by AstraZeneca Pharmaceuticals LP.

**Erwinaze™** (asparaginase Erwinia chrysanthemi), an asparaginase enzyme, was approved to treat patients with acute lymphoblastic leukemia (ALL), who have developed an allergy or hypersensitivity to E. coli-derived asparaginase and pegaspargase chemotherapy drugs used to treat ALL. It is the first and only alternative approved for patients with hypersensitivity to “standard-of-care” treatment. It is estimated that 15 percent to 20 percent of ALL patients develop hypersensitivity to E. coli-derived asparaginase.

ALL is the most common form of childhood cancer, affecting about 2,900 children each year. Erwinaze is injected directly into the muscle three times a week and works by depleting the levels of asparagine (a protein building block) in the blood. Asparagine is essential for cell growth, and its removal from the blood inhibits the growth of ALL cells. It kills the leukemia cells while normal cells are able to make enough asparagine and are not affected by the treatment.

Erwinaze was developed by EUSA Pharma (USA), Inc.

**Jakafi™** (ruxolitinib tablets) is the first and only treatment specifically approved for myelofibrosis, a life-threatening blood cancer. It is indicated for patients with intermediate or high-risk myelofibrosis, which accounts for 80 percent to 90 percent of all myelofibrosis patients. Jakafi is the first in a new class of medicines called Janus kinase (JAK) inhibitors. It inhibits the enzymes JAK 1 and JAK 2 that are involved in regulating blood and immunological functioning and are associated with myelofibrosis.

Jakafi was developed by Incyte Corporation.
**Cardiovascular Diseases**

Three new medicines for cardiovascular disease were approved, including one for acute coronary syndrome and one for the prevention of deep vein thrombosis.

**Brilinta™** (ticagrelor tablets), an oral anticoagulant, was approved to reduce cardiovascular death and heart attack in patients with acute coronary syndrome (ACS). ACS is a group of symptoms for conditions, including unstable angina and heart attack, which result in insufficient blood supply to the heart muscle. Brilinta works by blocking the formation of new blood clots and maintaining blood flow to help reduce a patient’s risk of cardiovascular events.

In clinical trials in combination with aspirin, Brilinta was more effective in preventing heart attacks and death when compared to an existing medicine.

Brilinta was developed by AstraZeneca Pharmaceuticals LP.

**Edarbi™** (azilsartan medoxomil), a once-daily oral medicine, was approved for the treatment of hypertension. Edarbi is an angiotensin II receptor blocker that lowers blood pressure by blocking the action of angiotensin II, a vasopressor hormone that constricts blood vessels. When the angiotensin II receptor is blocked, blood vessels stay relaxed and open, and blood pressure can be reduced.

In clinical trials, Edarbi was more effective in lowering 24-hour blood pressure compared to two FDA-approved antihypertensive drugs.

Edarbi was developed by Takeda Global Research & Development Center, Inc., and will be marketed by Takeda Pharmaceutical North America, Inc.

**Xarelto®** (rivaroxaban tablets), a once-daily anticoagulant, was approved for the prevention of deep vein thrombosis which may lead to pulmonary embolism in patients undergoing knee or hip replacement surgery. It works by blocking the blood clotting factor IX and thereby reducing the formation of blood clots.

Xarelto was developed by Janssen Pharmaceuticals, Inc.

**Depression**

**Viibryd®** (vilazodone HCl) was approved for the treatment of major depressive disorder (MDD) in adults. MDD is caused by a chemical imbalance in the brain. Viibryd is the first and only selective serotonin reuptake inhibitor and 5HT1A receptor partial agonist combination. Viibryd works by enhancing serotonin in the brain by selectively inhibiting serotonin reuptake. Nearly 18 million people in the United States suffer from MDD.

Viibryd was developed by Forest Laboratories, Inc.

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**Xalkori®** (crizotinib), a personalized medicine, is the first and only treatment specifically approved for patients with locally advanced or metastatic ALK-positive (anaplastic lymphoma kinase) non-small-cell lung cancer (NSCLC). Xalkori acts by blocking signaling in a number of cell pathways that are believed to be critical for the growth and survival of tumor cells, leading to stabilization or regression of tumors. It was approved with a first-of-its-kind companion diagnostic test (Vysis ALK Break Apart FISH Probe Kit) to help determine if the patient has the abnormal ALK gene, which promotes cancer cell growth. About 1 percent to 7 percent of NSCLC cases have the gene abnormality.

Xalkori was developed by Pfizer Inc.

**Yervoy™** (ipilimumab), a cancer immunotherapy, was approved for the treatment of unresectable or metastatic melanoma and is the first approved for melanoma in 13 years. It is a monoclonal antibody that binds to and blocks the activity of cytotoxic T-lymphocyte antigen-4 (CTLA-4), a negative regulator of T-cell activation that may cause the immune system to slow down or turn off, affecting the body’s ability to fight cancer cells. It is believed that by blocking CTLA-4 activity, Yervoy can help the immune system attack cancer cells in melanoma tumors. Melanoma is the leading cause of death from skin disease, with more than 76,000 new cases and more than 9,000 deaths expected this year in the United States.

Yervoy was developed by Bristol-Myers Squibb Company.

**Zelboraf®** (vemurafenib tablets), a personalized medicine, was approved for the treatment of unresectable or metastatic melanoma that expresses a gene mutation called BRAF V600E. It was approved with a first-of-a-kind companion diagnostic (4800 BRAF V600 Mutation Test) to help determine if a patient has the gene mutation. The BRAF protein is normally involved in regulating cell growth but is mutated in about half of the late-stage melanoma cases. Zelboraf inhibits BRAF and is able to block the function of the V600E-mutated BRAF protein.

Zelboraf was developed by Genentech USA, Inc., a member of the Roche Group.

**Zytiga®** (abiraterone acetate tablets) was approved in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer in patients who have had previous chemotherapy containing docetaxel. It is the first once-daily, oral treatment for metastatic prostate cancer and inhibits androgen production at all three sources—the testes, the adrenal glands, and in men with prostate cancer, the tumor tissue itself. Androgens are hormones that promote the development and maintenance of male sex characteristics. In prostate cancer, the androgens can help to fuel the tumor’s growth. This year, in the United States, more than 241,000 men are expected to be diagnosed with prostate cancer and more than 21,000 are expected to die from the disease.

Zytiga was developed by Janssen Biotech, Inc.
A Look at the New Drugs and Biologics Approved in 2011

**Diabetes**

**Tradjenta™ (linagliptin)** was approved for the treatment of type 2 diabetes. It is the first dipeptidyl peptidase-4 (DPP-4) to be approved at one dosage strength, meaning there is no dose adjustment recommended for patients with kidney or liver impairment.

In type 2 diabetes, people do not produce enough insulin, a hormone that regulates blood glucose levels. Tradjenta lowers blood sugar by increasing incretin levels, which increase insulin levels after meals and throughout the day.

Type 2 diabetes is the most common form of diabetes, affecting 90 percent to 95 percent of the 24 million Americans with diabetes.

Tradjenta was developed by Boehringer Ingelheim Pharmaceuticals, Inc., and Eli Lilly and Company.

**Eye Disorders**

**Eylea® (aflibercept injection)**, a recombinant fusion protein, was approved for the treatment of wet (neovascular) age-related macular degeneration (AMD), a leading cause of vision loss and blindness in older Americans. There are two forms of AMD, wet or dry. In wet AMD, new blood vessels grow beneath the retina and leak blood and fluid. This leakage causes dysfunction in the retina leading to visual distortion and/or blind spots in central vision, which allows the eye to see fine detail.

Vascular endothelial growth factor (VEGF) is a naturally occurring protein in the body that triggers the formation of new blood vessels supporting the growth of the body's tissues and organs. In wet AMD, VEGF is associated with the growth of abnormal new blood vessels in the eye, leading to fluid in the macula. Eylea binds to VEGF and inhibits the growth of blood vessels.

Eylea was developed by Regeneron Pharmaceuticals in collaboration with Bayer HealthCare Pharmaceuticals.

**Genetic Disorders**

Three new medicines were approved for genetic disorders, including the first treatment for hereditary angioedema.

**Corifact®** (factor XIII concentrate [human]) was approved for the treatment of congenital factor XIII deficiency, a rare and potentially life-threatening bleeding disorder. It is the first and only FXIII concentrate approved in the United States. Congenital FXIII deficiency is a disorder where the blood clots formed are unstable, leading to recurrent bleeding. It is estimated that it affects one person in 2 million, with incidence in the United States about 150 people. In clinical trials, Corifact was shown to immediately increase FXIII levels in the blood.

Corifact was developed by CSL Behring.

**Ferriprox® (deferiprone)** was approved for the treatment of iron overload due to blood transfusions in patients with thalassemia who had an inadequate response to prior chelation therapy. It is the first new drug approved for this disorder since 2005. Iron overload can lead to organ failure and early death. Patients with thalassemia, a genetic disorder that causes anemia, have excess iron in the body from frequent blood transfusions. Standard treatment of iron overload is chelation therapy by which chemical agents are used to remove heavy metals from the body.

Ferriprox was developed by ApoPharma, Inc.

**Firazyr® (icatibant injection)** was approved for the treatment of acute attacks of hereditary angioedema (HAE) in adults. It is the first and only self-administered treatment approved for HAE. HAE is a rare genetic disease caused by low levels or a dysfunction of C1 esterase inhibitor (C1-INH) and is characterized by recurrent, sometimes disfiguring and often painful episodes of acute swelling which can be life-threatening.

Firazyr can be carried and stored at room temperature and self-injected, allowing for fast treatment without having to travel to a healthcare provider for treatment.

Firazyr was developed by Shire Human Genetic Therapies, Inc.

**Imaging Agents**

Two new imaging agents were approved, including the first for neurodegenerative movement disorders.

**DaTscan™ (loflupane I-123 injection)** is the first diagnostic imaging approved for evaluation of neurodegenerative movement disorders, specifically for differentiating between Parkinsonian syndromes and essential tremor. DaTscan is a radiopharmaceutical imaging agent that works by binding to dopamine transporters (DaT) in the brain. A specific marker for DaT, it produces images that provide visual evidence of the presence of dopamine transporters. Parkinsonian syndromes are a group of neurodegenerative disorders characterized by rigidity, tremor, and impaired ability to walk.

DaTscan was developed by GE Healthcare.

**Gadavist™ (gadobutrol injection)**, a gadolinium-based contrast agent, was approved for intravenous use in diagnostic magnetic resonance imaging (MRI) in adults and children (2 years of age and older) to detect and visualize areas with disrupted blood brain barrier and/or abnormal blood supply and circulation of the central nervous system.

Gadavist was developed by Bayer HealthCare Pharmaceuticals, Inc.
Infectious Diseases

Six medicines for infectious diseases were approved, including the first antibacterial approved for *Clostridium difficile*-associated diarrhea in nearly 30 years and two new hepatitis C treatments.

Ardovax™ (adenovirus type 4 and type 7 vaccine, live, oral) was approved for the active immunization to prevent febrile acute respiratory disease (ARD) caused by adenovirus type 4 and type 7. It will be used in military populations ages 17 through 50. The vaccine was developed by Teva North America.

Dificid® (fidaxomicin tablets), an oral medication, was approved for the treatment of *Clostridium difficile*-associated diarrhea (CDAD) in adults. It is the first antibacterial medicine indicated for CDAD in nearly 30 years. CDAD is a serious illness resulting from infection of the colon by *C. difficile* bacteria, which produce toxins that cause inflammation of the colon, severe diarrhea and, in severe cases, death. CDAD affects more than 700,000 people each year in the United States and is the leading cause of healthcare-acquired infections in community hospitals.

Dificid was developed by Optimer Pharmaceuticals, Inc.

Edurant® (rilpivirine tablets) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) indicated for the treatment of HIV infection in treatment-naïve adults (patients who have never been treated with HIV medication) in combination with other antiretroviral medications. NNTRIs are designed to block a specific protein that HIV-1 uses for replication.

Edurant was developed by Tibotec Pharmaceuticals and is distributed by Janssen Therapeutics, Division of Janssen Products, LP.

Incivek™ (telaprevir tablets) was approved for the treatment of chronic hepatitis C with compensated liver disease (some level of damage to the liver but the liver still functions) in combination with interferon therapy. It is an oral medicine that acts directly on the hepatitis C virus protease, the enzyme essential for viral replication. In clinical trials, 79 percent of people treated with Incivek achieved a viral cure. About 3.2 million people in the United States have chronic hepatitis C.

Incivek was developed by Vertex Pharmaceuticals Incorporated.

Natroba™ (spinosad topical suspension) was approved for the treatment of head lice infestation in patients four years of age and older. It does not require nit combing and in most cases successfully treats the infestation in one 10-minute application. Natroba was derived from a soil microbe.

Head lice are the second most common communicable disease in school-age children, after the common cold.

Natroba was developed by ParaPRO LLC.

Victrelis™ (boceprevir), a first-in-class medicine approved for the treatment of chronic hepatitis C with compensated liver disease in combination with interferon therapy. Victrelis is a hepatitis C protease inhibitor, which works by binding to the virus and preventing it from multiplying.

In clinical trials, two-thirds of patients experienced a significant increase in virologic response (hepatitis C was not detectable in the blood) when taking Victrelis in combination with pegylated interferon and ribavirin, compared to pegylated interferon and ribavirin alone (the current standard treatment).

Victrelis was developed by Merck & Co., Inc.

Neurological Disorders

Three new medicines were approved for neurological disorders, including one for Lennox-Gastaut syndrome, a very severe form of epilepsy most often diagnosed in children.

Horizant® (gabapentin enacarbil extended-release tablets) is the first medicine in its class to be approved for the treatment of moderate to severe primary restless legs syndrome. Horizant, a prodrug of the epilepsy treatment gabapentin, utilizes the body’s nutrient transport mechanisms that are believed to facilitate absorption into the body. Once absorbed, it is converted into gabapentin, which binds to a specific calcium channel but not others. Its exact mechanism of action against RLS is unknown.

Horizant was developed by XenoPort, Inc. and GlaxoSmithKline.

Onfi™ (clobazam), an oral antiepileptic, was approved for the adjunctive (add-on) treatment of seizures associated with Lennox-Gastaut syndrome in patients 2 years of age and older. Lennox-Gastaut syndrome is a severe form of epilepsy that causes debilitating seizures and affects fewer than 200,000 people in the United States.

Onfi was developed by Lundbeck, Inc.

Potiga™ (ezogabine tablets) was approved for the adjunctive treatment of partial-onset seizures in adults, the most common type of seizure associated with epilepsy. It is the first neuronal potassium channel opener developed for epilepsy. While the exact mechanism of action is not established, it may act as an anticonvulsant by stabilizing the neuronal potassium channels in an “open” position, thereby reducing excitability.

Potiga was developed by Valeant Pharmaceuticals North America and GlaxoSmithKline.
A Look at the New Drugs and Biologics Approved in 2011

Respiratory Disorders

Two medicines were approved for chronic obstructive pulmonary disease (COPD), including the first in a new class of drugs for the disease.

**Arcapta™ Neohaler™** (indacaterol inhalation powder) is the first and only once-daily, long-acting beta2-agonist (LABA) approved for the maintenance treatment of airflow in chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. COPD is the third leading cause of death in the United States, affecting more than 12 million Americans. Another 12 million remain undiagnosed.

In clinical trials, Arcapta significantly improved lung function at 24 hours after treatment, with initial improvement seen five minutes after the first dose. It also decreased the need for daily rescue medications.

Arcapta was developed by Novartis Pharmaceuticals Corporation.

**Daliresp®** (roflumilast tablets) is the first in a new class of medicines approved to decrease the frequency of flare-ups (exacerbations) or worsening of symptoms associated with severe chronic obstructive pulmonary disease (COPD). It was approved to treat cough and excess mucus associated with chronic bronchitis, but not COPD associated with emphysema. Daliresp is an oral selective phosphodiesterase-4 (PDE-4) inhibitor.

In clinical trials, it demonstrated a significant reduction in the rate of moderate to severe exacerbations by 15 percent to 18 percent.

Daliresp was developed by Forest Laboratories, Inc.

Transplantation

**Nulojix®** (belatacept) is the first selective T-cell co-stimulation blocker approved for the prevention of acute rejection of kidney transplantation in adults in combination with other approved immunosuppressants. Nulojix inhibits T-cell proliferation. Activated T-cells play an important role in immunologic rejection. More than 89,000 patients are waiting for a kidney transplant in the United States, according to the Organ Procurement and Transplantation Network.

Nulojix was developed by Bristol-Myers Squibb.

Other

**Anascorp®** (Centruroides [Scorpion] immune F(ab’)2 [equine] injection) is the first specific treatment approved for scorpion stings. It is made from the plasma of horses that have been immunized with the scorpion’s venom and vaccinated against viruses that could infect humans. In clinical trials, the neurological signs of scorpion stings were resolved within four hours for eight of 15 subjects who received Anascorp, compared to one of seven who received the placebo. There were 17,000 reported scorpion stings in 2009. Scorpion stings can be life-threatening, especially in children.

Anascorp was developed by Instituto Biocon of Tlalpan, Mexico and licensed to Rare Disease Therapeutics, Inc.

**Kedbumin™** (albumin [human] sterile, aqueous solution for single dose intravenous administration) was approved to treat several diseases benefiting from albumin. It is indicated for the treatment of hypovolemic shock, hypoalbuminemia, ovarian hyperstimulation syndrome, adult respiratory distress syndrome, burns, hemodialysis patients undergoing long-term dialysis, patients who cannot tolerate substantial volumes of salt reduction, priming solution for cardiopulmonary bypass, and the prevention of central volume depletion after paracentesis due to cirrhotic ascites.

Kedbumin was developed by Kedrion of Barga (Lucca), Italy.

**laViv®** (azficel-T) is the first and only personalized aesthetic cell therapy approved by the FDA. It was approved for the improvement of the appearance of moderate to severe nasolabial fold wrinkles (smile lines) in adults. Personalized cell therapy uses a patient’s own cells to create the medicine. LaViv is created using collagen-producing skin cells (fibroblasts) taken from behind the patient’s ear and then cultured and frozen until treatment.

laViv was developed by Fibrocell Science, Inc. of Exton, Pennsylvania.
acutecoronary syndrome (ACS)—Acute coronary syndrome is a result of insufficient blood supply to the heart muscle caused by unstable angina and/or myocardial infarction (heart attack).

BLA (Biologic License Application)—Application submitted by a sponsor to the FDA for approval of a new biologic for sale and marketing in the United States.

chronic obstructive pulmonary diseases (COPD)—The combination of chronic bronchitis and emphysema, in which there is a persistent disruption of airflow out of the lungs and eventual hypoxemia (low level of oxygen in the blood).

cirrhotic ascites—The accumulation of fluid in the peritoneal cavity due to liver cirrhosis. Paracentesis refers to the procedure involving needle drainage of fluid from the peritoneal cavity in the abdomen.

Clostridium difficile—A bacterium that produces an irritating toxin that causes a form of colitis characterized by profuse, watery diarrhea with cramps and low-grade fever.

depression—A feeling of intense sadness, which may follow a recent loss or other sad event but is out of proportion to that event and persists beyond an appropriate length of time. Major depressive disorder (or major depression syndrome) includes an episode of depression defined as a persistent (for at least 2 weeks) mood disturbance, plus at least 4 of the following: sleep disturbance, changes in psychomotor activity, loss of ability to experience pleasure and interest, fatigue, feelings of worthlessness or guilt, difficulty in concentrating, and preoccupation with death or a wish to die. Major depression is associated with impairment in social functioning.

diabetes—A chronic disease in which the body does not produce or properly use insulin, a hormone that is needed to convert sugar, starches and other food into energy needed for daily life. Symptoms may include excessive thirst, hunger, urination and weight loss. The cause of diabetes continues to be a mystery, although both genetics and environmental factors such as obesity and lack of exercise appear to play roles. Type 2 diabetes results from insulin resistance (a condition in which the body fails to properly use insulin), combined with relative insulin deficiency. Most Americans who are diagnosed with diabetes have type 2, which in most cases can be controlled by a combination of dietary measures, weight loss, and oral medication.

type 2 diabetes—A chronic disease in which the body fails to properly use insulin, combined with relative insulin deficiency. Most Americans who are diagnosed with diabetes have type 2, which in most cases can be controlled by a combination of dietary measures, weight loss, and oral medication.

embolism—The obstruction of a blood vessel by a foreign substance or a blood clot. Foreign substances that can cause embolism include an air bubble, amniotic fluid, a globule of fat, a clump of bacteria, chemicals, and drugs. Blood clots are the most common cause of embolism. The term “embolus” refers to the substance or clot that is obstructing the blood vessel, while “embolism” refers to the process by which that happens. A pulmonary embolism occurs when the blood clot breaks off and travels to the lungs, where it can impact the flow of oxygenated blood and can potentially be life-threatening.

epilepsy—A brain disorder caused by abnormal or excessive electrical activity in the brain. A partial seizure, the most common type of seizure in epilepsy, affects only a limited or localized area of the brain. Symptoms of seizures include repetitive limb movements (spasms), unusual behavior, and generalized convulsions with loss of consciousness.

factor XIII deficiency—A rare, genetic defect, where patients do not make enough factor XIII, a substance that circulates in the blood and is important for normal clotting. The deficiency can cause soft tissue bleeding, mucosal bleeding, and fatal intracranial bleeding. Newborns with factor XIII deficiency may have umbilical cord bleeding.

febrile—Relating to or characterized by fever.

hemodialysis—A method of mechanically cleansing the blood outside of the body in order to remove various substances that would normally be cleared by the kidneys. Hemodialysis is used when an individual is in relative, or complete, kidney failure.

hepatitis—Inflammation of the liver accompanying liver cell damage or death, caused most often by viral infection, e.g., hepatitis A, B and C.

hereditary angioedema (HAE)—A rare genetic disease characterized by recurrent episodes of acute swelling which can be life-threatening in some cases. The swelling attacks can affect any part of the body, but most commonly occur in the face, gastrointestinal tract, extremities, or genitals. Attacks can be disfiguring and painful.

HIV infection—Presence of antibodies in the blood to the human immunodeficiency virus (the virus that causes AIDS). HIV-1 refers to the most common strain of the virus found in U.S. AIDS patients.

hypertension—Persistent elevation of blood pressure above the normal range while the heart is in systolic (contracting) or diastolic (relaxed) mode. Uncontrolled, chronic hypertension strains the heart, damages arteries and creates a greater risk of heart attack, stroke and kidney problems.

hypoalbuminemia—A condition marked by abnormally low amounts of the body’s main serum-binding protein, albumin. Insufficient albumin can lead to edema and platelet malfunction.

hypovolemic shock—An emergency condition in which severe blood and fluid loss makes the heart unable to pump enough blood to the body. This type of shock can cause many organs to stop working.

imaging agent—A substance used to enhance x-ray images of organs and spaces in the body.
Melanoma is the most dangerous type of skin cancer made up of pigmented (usually brown-colored) skin cells anywhere in the body. Melanoma is the most dangerous type of skin cancer.

metastases—Areas of secondary cancer that have spread from the primary or original cancer site.

MRI—Magnetic resonance imaging.

myelofibrosis—a blood cancer in which the bone marrow is replaced by scar tissue resulting in blood cells being made in organs such as the liver and spleen. It is characterized by bone marrow failure, enlarged spleen, and debilitating symptoms such as fatigue, severe itching, night sweats, bone pain, and an early feeling of fullness. It belongs to a group of diseases referred to as myeloproliferative neoplasms.

nasolabial fold wrinkles—Smile lines.

NDA (New Drug Application)—Application submitted by a sponsor to the FDA for approval of a new pharmaceutical for sale and marketing in the United States.

NME (new molecular entity)—The U.S. Food and Drug Administration classifies a drug as an NME if the active ingredient has never been previously marketed in the United States for use in a drug product either as a single agent or part of a combination.

non-small-cell lung cancer (NSCLC)—Lung cancer is the leading cause of cancer death in the United States. NSCLC accounts for 85 percent to 90 percent of lung cancers.

Orphan Drug—A drug to treat a disease that has a patient population of 200,000 or less, or a disease that has a patient population of more than 200,000 and a developmental cost that will not be recovered from sales in the United States.

PD (Parkinson’s disease)—PD belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells. The four primary symptoms of PD are tremor, or trembling in hands, arms, legs, jaw, and face; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance and coordination. PD is both chronic, meaning it persists over a long period of time, and progressive, meaning its symptoms grow worse over time. As these symptoms become more pronounced, patients may have difficulty walking, talking, or completing other simple tasks. Early symptoms of PD are subtle and occur gradually. In some people, the disease progresses more quickly than in others. As the disease progresses, the tremor, which affects the majority of PD patients, may begin to interfere with daily activities. Other symptoms may include depression and other emotional changes, difficulty in swallowing, chewing, and speaking; urinary problems or constipation; skin problems; and sleep disruptions. Although some people become severely disabled, others experience only minor motor disruptions. No one can predict which symptoms will affect an individual patient, and the intensity of the symptoms also varies from person to person.

pediculosis—Infestation with lice, which are ectoparasites that live on the body. The three types of lice that infect humans are: Pediculus humanus capitis (head louse), Pediculus humanus corporis (body louse), and Phthirus pubis (pubic louse). The lice are spread from person to person by close physical contact or through objects such as combs and clothes. The body louse is the vector of typhus, trench fever, and relapsing fever.

personalized medicine—Is the tailoring of medical treatment to the individual characteristics of each patient. The approach relies on scientific breakthroughs in our understanding of how a person’s unique molecular and genetic profile makes them susceptible to certain diseases. This same research is increasing
our ability to predict which medical treatments will be safe and effective for each patient, and which ones will not be. Personalized medicine may be considered an extension of traditional approaches to understanding and treating disease. Equipped with tools that are more precise, physicians can select a therapy or treatment protocol based on a patient’s molecular profile that may not only minimize harmful side effects and ensure a more successful outcome, but can also help contain costs compared with a “trial-and-error” approach to disease treatment.

prostate cancer—A cancer where the male hormone testosterone stimulates prostate tumors to grow. Treatments are used to reduce testosterone production or to block its effects. In castration-resistant prostate cancer, the tumors continue to grow even when testosterone levels are low.

respiratory distress syndrome—A life-threatening lung condition that prevents enough oxygen from getting into the blood. In adults it is caused by inflammation or injury to the lungs, leading to a buildup of fluid in the air sacs. Inflammation and injury can be caused by aspirating vomit into the lungs, inhaling chemicals, pneumonia, septic shock, and trauma. Symptoms include labored breathing, low blood pressure, organ failure, and shortness of breath.

restless legs syndrome—Restless legs syndrome is an overwhelming urge to move the legs usually caused by uncomfortable or unpleasant sensations in the legs. The sensations have the following features: occur during periods of inactivity; become more sensitive in the evening and at night; are relieved by movement of the limb; often cause difficulty staying or falling asleep, which leads to feelings of daytime tiredness or fatigue; and may cause involuntary jerking of the limbs during sleep and sometimes during wakefulness.

scorpion stings—Most scorpion stings in the United States cause only minor signs and symptoms, such as pain and warmth at the sting site. The venom of the bark scorpion, which is native to Arizona, New Mexico, and the California side of the Colorado River, is more toxic and can be life-threatening, particularly in children. Children who have been stung by a bark scorpion might experience pain, which can be intense, numbness and tingling in the area around the sting, but little or no swelling; muscle twitching or thrashing; unusual head, neck and eye movements; drooling; sweating; and restlessness or excitability and sometimes inconsolable crying. Adults are more likely to experience: rapid breathing, high blood pressure, increased heart rate, muscle twitching and weakness.

SPECT imaging—Single-photon emission computed tomography (SPECT) is an imaging technique using gamma rays and is able to provide 3D images.

stem cell transplantation, hematopoietic—Stem cell transplantation is used in patients with disorders affecting the hematopoietic (blood forming) system, such as hematologic malignancies, primary immunodeficiency diseases, bone marrow failure, and beta-thalassemia.

systemic—Affecting the whole body.

systemic lupus erythematosus—A chronic autoimmune disorder, affecting many systems of the body, including the kidneys and brain.

thalassemia—A genetic blood disorder that causes anemia. The blood transfusions used to treat the disorder cause excess iron in the body, a serious and possibly fatal condition. Patients are at risk for liver disease, diabetes, arthritis, heart failure or an abnormal heart rhythm.

thyroid cancer—Thyroid cancer affects the thyroid gland (located in the neck). Medullary thyroid cancer involves specific types of cells that are found in the thyroid gland and can occur spontaneously or as part of a genetic syndrome. More than 44,000 new cases of thyroid cancer are diagnosed each year. Medullary thyroid cancer accounts for an estimated 3 percent to 5 percent of all thyroid cancers. Common symptoms include coughing, difficulty swallowing, enlargement of the thyroid gland, swelling of the neck, a lump on the thyroid, and changes in voice or hoarseness.
PhRMA Member Companies Invested $49.5 Billion In Research and Development in 2011

Investment in research and development by members of the Pharmaceutical Research and Manufacturers of America (PhRMA) remained strong at $49.5 billion in 2011, as the sector adapts to meet the challenges of evolving science, a changing marketplace and a difficult economic environment.

Biopharmaceutical research companies are continuing to explore the possibilities associated with more targeted therapies and personalized medicines, and are building on the benefits associated with partnerships among experts throughout the research ecosystem.

The 2011 R&D investment figures reflect the biopharmaceutical sector’s standing as America’s most research-intensive industry. According to a recent report by the National Science Board of the National Science Foundation, the U.S. biopharmaceutical sector accounts for the single largest share of all U.S. business R&D, representing nearly 20 percent of all domestic R&D funded by U.S. businesses. In the U.S., R&D expenditures among PhRMA members represented a remarkable 21.1 percent of domestic sales.

Despite facing market, scientific and regulatory challenges, the U.S. biopharmaceutical sector—led by PhRMA member companies—has remained a major contributor to American innovation.

PhRMA member companies’ investment represents a boost to America’s economy, with 78 percent of those dollars invested on our shores. But more importantly, it shows a continued commitment to medical progress that will continue to bring new solutions to America’s patients.

The remarkable breakthroughs achieved in 2011 are a testament to our greater understanding of the molecular and genetic basis of disease. As our knowledge and research capabilities grow, PhRMA member com-

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### Domestic R&D and R&D Abroad**, PhRMA Member Companies: 1970-2011

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* Estimated

** R&D abroad includes expenditures outside of the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by U.S. divisions of foreign-owned PhRMA member companies. R&D performed abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic R&D, however, includes R&D expenditures within the United States by all PhRMA member companies.

*** R&D abroad affected by merger and acquisition activity.

Notes: All figures include company-financed R&D only. Total values may be affected by rounding.

PhRMA Member Companies Invested $49.5 Billion In Research and Development in 2011

<table>
<thead>
<tr>
<th>Year</th>
<th>Domestic R&amp;D</th>
<th>Annual Percentage Change</th>
<th>R&amp;D Abroad</th>
<th>Annual Percentage Change</th>
<th>Total R&amp;D</th>
<th>Annual Percentage Change</th>
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</tbody>
</table>

* Estimated
** Sales abroad includes sales generated outside the United States by U.S.-owned PhRMA member companies and sales generated abroad by U.S. divisions of foreign-owned PhRMA member companies. Sales generated abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic sales, however, includes sales generated within the United States by all PhRMA member companies.
*** Revised in 2007 to reflect updated data.
**** Sales abroad affected by merger and acquisition activity.
Notes: Total values may be affected by rounding.

PhRMA member companies are able to use those advances to develop more targeted and effective therapies, a new generation of treatments for the most costly and challenging diseases. According to a survey conducted by the Tufts University Center for the Study of Drug Development, 94 percent of surveyed companies are currently investing in the field of personalized medicine.

Beyond the impressive numbers reported by our member companies is the unfolding story of how companies are adapting to a changing research paradigm. Part of that story is our shift to a more agile sector, which increasingly involves collaborative, constructive partnerships with both public and private experts.

The growing complexity of science requires access to broader expertise. These partnerships—which can involve experts from across the healthcare spectrum, including academia, government-funded research, and of course other biopharmaceutical companies—help companies build upon a larger reservoir of knowledge.

Other steps that companies are taking include identifying efficiencies and reorganizing research structures throughout the R&D process and improving productivity and achieving other efficiencies through incorporation of new technologies.

By continuing to explore enhancements to their R&D and manufacturing approaches, PhRMA member companies are striving to turn compounds in their ever-growing pipelines into medical breakthroughs for the good of patients across the world. Today, there are more than 3,200 medicines in clinical trials or undergoing FDA review in the U.S., up from 2,400 in 2005.
PhRMA Member Companies Invested $49.5 Billion In Research and Development in 2011

R&D Investments by PhRMA Member Companies, 1987-2011

Expenditures ($ billions)

R&D as a Percentage of Sales, PhRMA Member Companies: 1970-2011

<table>
<thead>
<tr>
<th>Year</th>
<th>Domestic R&amp;D as a % of Domestic Sales</th>
<th>Total R&amp;D as a % of Total Sales</th>
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</thead>
<tbody>
<tr>
<td>2011</td>
<td>21.1%</td>
<td>16.7%</td>
</tr>
<tr>
<td>2010</td>
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<td>2008</td>
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<tr>
<td>2006</td>
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<tr>
<td>2004</td>
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<td>1970</td>
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<td>9.3%</td>
</tr>
</tbody>
</table>

* Estimated
** Revised in 2007 to reflect updated data.
Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2012

* Estimated
Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2012
It takes 10-15 years on average for an experimental drug to travel from the lab to U.S. patients. Only five in 5,000 compounds that enter preclinical testing make it to human testing. One of these five tested in people is approved.

**The Drug Development and Approval Process**

The U.S. system of new drug approvals is perhaps the most rigorous in the world. It takes 10-15 years, on average, for an experimental drug to travel from the laboratory to U.S. patients, according to the Tufts Center for the Study of Drug Development. Only five in 5,000 compounds that enter preclinical testing make it to human testing. And only one of those five is approved for sale.

On average, it costs a company $1.2 billion, including the cost of failures, to get one new medicine from the laboratory to U.S. patients, according to a 2007 study by the Tufts Center for the Study of Drug Development.

Once a new compound has been identified in the laboratory, medicines are usually developed as follows:

**Preclinical Testing.** A pharmaceutical company conducts laboratory and animal studies to show biological activity of the compound against the targeted disease, and the compound is evaluated for safety.

**Investigational New Drug Application (IND).** After completing preclinical testing, a company files an IND with the U.S. Food and Drug Administration (FDA) to begin to test the drug in people. The IND shows results of previous experiments; how, where and by whom the new studies will be conducted; the chemical structure of the compound; how it is thought to work in the body; any toxic effects found in the animal studies; and how the compound is manufactured. All clinical trials must be reviewed and approved by the Institutional Review Board (IRB) where the trials will be conducted. Progress reports on clinical trials must be submitted at least annually to FDA and the IRB.

**Clinical Trials, Phase I.** These tests usually involve about 20 to 100 healthy volunteers. The tests study a drug’s safety profile, including the safe dosage range. The studies also determine how a drug is absorbed, distributed, metabolized, and excreted as well as the duration of its action.

**Clinical Trials, Phase II.** In this phase, controlled trials of approximately 100 to 500 volunteer patients (people with the disease) assess a drug’s effectiveness and determine the early side effect profile.

**Clinical Trials, Phase III.** This phase usually involves 1,000 to 5,000 patients in clinics and hospitals. Physicians monitor patients closely to confirm efficacy and identify adverse events.

**New Drug Application (NDA)/Biologic License Application (BLA).** Following the completion of all three phases of clinical trials, a company analyzes all of the data and files an NDA or BLA with FDA if the data successfully demonstrate both safety and effectiveness. The applications contain all of the scientific information that the company has gathered. Applications typically run 100,000 pages or more.

**Approval.** Once FDA approves an NDA or BLA, the new medicine becomes available for physicians to prescribe. A company must continue to submit periodic reports to FDA, including any cases of adverse reactions and appropriate quality-control records. For some medicines, FDA requires additional trials (Phase IV) to evaluate long-term effects.

Discovering and developing safe and effective new medicines is a long, difficult, and expensive process. PhRMA member companies invested an estimated $49.5 billion in research and development in 2011.