

2011

New Drug Approvals in 2010

PRESENTED BY AMERICA'S BIOPHARMACEUTICAL RESEARCH COMPANIES

Biopharmaceutical Research Companies Receive Approval for 26 New Treatments in 2010

America's biopharmaceutical research companies obtained approval for 26 new medicines in 2010 from the U.S. Food and Drug Administration (FDA).

The medicines include 15 new drugs (also called new molecular entities or NMEs), six therapeutic biologics, and five other biologics. Among the medicines:

- A new medicine for the prevention of itching associated with allergic conjunctivitis.
- Four medicines to treat musculoskeletal disorders, including a first-in-class, twice-a-year medicine for the prevention of osteoporosis.
- Three new medicines to treat cancer—two for prostate cancer and one for breast cancer—including the first immunotherapy that uses a patient's own immune cells to stimulate their immune system to fight the cancer.
- Two new contraceptives, including one for emergency use.
- A new non-insulin once-daily medicine for the treatment of type 2 diabetes.
- Five treatments for five separate genetic disorders, including the first and only liquid treatment for a deficiency that causes congenital emphysema.
- Two vaccines and one infectious disease therapeutic, including a new vaccine which expands on an existing vaccine, extending coverage from seven serotypes of the bacterium to 13.
- A new once-daily medicine for the treatment of schizophrenia.
- Three new medicines for neurological disorders, including the first treatment to help improve walking in adults with multiple sclerosis and the first oral medicine to reduce relapses and delay disability progression in multiple sclerosis.
- The first anticoagulant approved in 50 years to prevent stroke.
- A new medicine to treat small varicose veins.
- The first treatment for HIV-related lipodystrophy.

Overall, the FDA approved 101 new therapeutics—the 15 NMEs, 11 biologics, and 75 additional novel medicines.

Detailed descriptions of the 26 medicines approved in 2010 begin on page six.

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 2010, PhRMA members alone invested an estimated \$49.4 billion in discovering and developing new medicines. Industry-wide research and investment reached \$67.4 billion in 2010. (See page 13 for more information on R&D and sales.) In addition, it 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 2010, the 21 new therapeutics approved by FDA's Center for Drug Evaluation and Research (CDER) were reviewed in an average of 14.8 months. Additionally, the five new products approved by FDA's Center for Biologics Evaluation and Research (CBER) in 2010 were reviewed in an average of 11.1 months.

As in past years, the number of potential new drugs entering clinical testing is increasing. 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 disease and illness.

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 get the medicines they need. Since April 2005, PPA has matched nearly 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.

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



Sincerely,
John J. Castellani
President and CEO
PhRMA

New Drug and Therapeutic Biological Approvals in 2010*

Product	Company	Indication/Use	NDA/BLA Received	FDA Approved	Review Time
Actemra® tocilizumab (S)	Genentech South San Francisco, CA	treatment of moderate to severe rheumatoid arthritis in adults	11/19/2007† 7/9/2009	1/8/2010	25.7 months
<i>For more information, contact: Genentech at (800) 626-3553 or www.actemra.com</i>					
Ampyra® dalfampridine extended-release tablets (P) (Orphan Drug)	Acorda Therapeutics Hawthorne, NY	treatment to improve walking in patients with multiple sclerosis	4/22/2009	1/22/2010	9.1 months
<i>For more information, contact: Acorda Therapeutics at (914) 347-4300 or www.ampyra.com</i>					
Asclera® polidocanol injection (S)	Chemische Fabrik Kreussler Weisbaden, Germany Merz Aesthetics San Mateo, CA	treatment of small varicose veins	9/29/2003†† 7/10/2009	3/30/2010	78.0 months
<i>For more information, contact: Merz Aesthetics at www.merzaesthetics.com or www.asclera.com</i>					
Carbaglu® carglumic acid (P) (Orphan Drug)	Orphan Europe Paris, France	treatment of NAGS deficiency (N-acetylglutamate synthase)	6/18/2009	3/18/2010	9.0 months
<i>For more information, contact: Orphan Europe at www.orphan-europe.com or www.carbaglu.net</i>					
Egrifta™ tesamorelin for injection (S)	EMD Serono Rockland, MA Theratechnologies Montreal, Canada	treatment of HIV-related lipodystrophy	5/29/2009	11/10/2010	17.5 months
<i>For more information, contact: EMD Serono at (800) 283-8088 or www.egrifta.com</i>					
ella® ulipristal acetate tablet (S)	HRA Pharma Paris, France Watson Pharmaceuticals Morristown, NJ	emergency contraception	10/15/2009	8/13/2010	10.0 months
<i>For more information, contact: Watson Pharmaceuticals at (800) 249-5499 or www.ellainfo.com</i>					
Gilenya™ fingolimod capsules (P)	Novartis Pharmaceuticals East Hanover, NJ	treatment of relapsing forms of multiple sclerosis	12/21/2009	9/21/2010	8.7 months
<i>For more information, contact: Novartis Pharmaceuticals at (888) 669-6682 or www.gilenya.com</i>					

* Approved by the Center for Drug Evaluation and Review (CDER).

(S) – Standard Review

(P) – Priority Review

† Original submission was made on 11/19/2007; a complete response to previous action was made on 7/9/2009; review time was calculated from 11/19/2007.

†† Original submission was made on 9/29/2003; a complete response to previous action was made on 7/10/2009; review time was calculated from 9/29/2003.

Product	Company	Indication/Use	NDA/BLA Received	FDA Approved	Review Time
Halaven™ eribulin mesylate injection (P)	Eisai <i>Woodcliff Lake, NJ</i>	treatment of late-stage metastatic breast cancer	3/30/2010	11/15/2010	4.6 months
<i>For more information, contact: Eisai at (888) 422-4743 or www.halaven.com</i>					
Jevtana® cabazitaxel injection (P)	sanofi-aventis <i>Bridgewater, NJ</i>	treatment of metastatic hormone-refractory prostate cancer	3/31/2010	6/17/2010	2.6 months
<i>For more information, contact: sanofi-aventis at (800) 633-1610 or www.jevtana.com</i>					
Krystexxa™ pegloticase (P) (Orphan Drug)	Savient Pharmaceuticals <i>East Brunswick, NJ</i>	treatment of chronic gout in adults	10/31/2008	9/14/2010	22.5 months
<i>For more information, contact: Savient Pharmaceuticals at (888) 579-7839 or www.krystexxa.com</i>					
Lastacaft™ alcaftadine ophthalmic solution 0.25% (S)	Allergan <i>Irvine, CA</i> Vistakon Pharmaceuticals <i>Jacksonville, FL</i>	prevention of itching associated with allergic conjunctivitis	9/29/2009	7/28/2010	10.0 months
<i>For more information, contact: Allergan at (800) 433-8871 or www.lastacaft.com</i>					
Latuda® lurasidone (S)	Sunovion Pharmaceuticals <i>Marlborough, MA</i>	treatment of schizophrenia in adults	12/30/2009	10/28/2010	10.0 months
<i>For more information, contact: Sunovion Pharmaceuticals at (508) 481-6700 or www.latuda.com</i>					
Lumizyme® alglucosidase alfa (P) (Orphan Drug)	Genzyme <i>Cambridge, MA</i>	treatment of late-onset Pompe disease	5/30/2008	5/24/2010	23.9 months
<i>For more information, contact: Genzyme at (617) 252-7500 or www.lumizyme.com</i>					
Natazia™ estradiol valerate and estradiol valerate/dienogest (S)	Bayer Healthcare Pharmaceuticals <i>Wayne, NJ</i>	contraception	7/6/2009	5/6/2010	10.0 months
<i>For more information, contact: Bayer Healthcare at (888) 842-2937 or www.natazia.com</i>					
Pradaxa® dabigatran etexilate capsules (P)	Boehringer Ingelheim Pharmaceuticals <i>Ridgefield, CT</i>	prevention of stroke and embolism in atrial fibrillation	4/19/2010	10/19/2010	6.0 months
<i>For more information, contact: Boehringer Ingelheim at (203) 798-9988 or www.pradaxa.com</i>					
Prolia® denosumab injection (S)	Amgen <i>Thousand Oaks, CA</i>	treatment of post-menopausal osteoporosis	12/19/2008	6/1/2010	17.4 months
<i>For more information, contact: Amgen at (800) 772-6436 or www.prolia.com</i>					

Product	Company	Indication/Use	NDA/BLA Received	FDA Approved	Review Time
Teflaro™ ceftaroline fosamil for injection (S)	Cerexa <i>Oakland, CA</i> Forest Laboratories <i>New York, NY</i>	treatment of bacterial infections	12/30/2009	10/29/2010	10.0 months
<i>For more information, contact: Forest Laboratories at (800) 678-1605 or www.teflaro.com</i>					
Victoza® liraglutide (rDNA origin) injection (S)	Novo Nordisk <i>Princeton, NJ</i>	treatment of type 2 diabetes	7/8/2009	1/25/2010	6.6 months
<i>For more information, contact: Novo Nordisk at (877) 484-2869 or www.victoza.com</i>					
Vpriv® velaglucerase alfa for injection (P) (Orphan Drug)	Shire Human Genetic Therapies <i>Cambridge, MA</i>	treatment of type 1 Gaucher disease	8/31/2009	2/26/2010	5.9 months
<i>For more information, contact: Shire Human Genetic Therapies at (866) 888-0660 or www.vpriv.com</i>					
Xeomin® incobotulinum- toxinA (S)	Merz Pharmaceuticals <i>Greensboro, NC</i>	treatment of cervical dystonia and blepharospasm	7/2/2009	7/30/2010	12.9 months
<i>For more information, contact: Merz Pharmaceuticals at (888) 637-9872 or www.xeomin.com</i>					
Xiaflex® collagenase clostridium histolyticum (P) (Orphan Drug)	Auxilium Pharmaceuticals <i>Malvern, PA</i>	treatment of Dupuytren's contracture	2/27/2009	2/2/2010	11.2 months
<i>For more information, contact: Auxilium Pharmaceuticals at (877) 942-3539 or www.xiaflex.com</i>					

New Biological Approvals in 2010*

Product	Company	Indication/Use	NDA/BLA Received	FDA Approved	Review Time
Glassia™ alpha1 proteinase inhibitor, human (S)	Kamada <i>Ness Ziona, Israel</i> Baxter International <i>Deerfield, IL</i>	treatment of alpha-1 antitrypsin deficiency	5/29/2009	7/1/2010	13.1 months
<i>For more information, contact: Baxter at (800) 422-9837 or www.myglassia.com</i>					

* Approved by the Center for Biologics Evaluation and Review.
(S) – Standard Review
(P) – Priority Review

Product	Company	Indication/Use	NDA/BLA Received	FDA Approved	Review Time
Hizentra® immune globulin subcutaneous (human), 20% liquid (S)	CSL Behring <i>King of Prussia, PA</i>	treatment of primary immunodeficiency disease	4/30/2009	3/4/2010	10.1 months
<i>For more information, contact: CSL Behring at (610) 878-4000 or www.hizentra.com</i>					
Menveo® meningococcal (groups A,C,Y, and W-135) oligosaccharide diphtheria CRM ₁₉₇ conjugate vaccine (S)	Novartis Vaccines & Diagnostics <i>Cambridge, MA</i>	for active immunization to prevent meningococcal disease	8/28/2008	2/19/2010	18.8 months
<i>For more information, contact: Novartis Vaccines & Diagnostics at (800) 244-7668 or www.menveo.com</i>					
Prevnar 13® pneumococcal 13-valent conjugate vaccine (diphtheria CRM ₁₉₇ protein) (P)	Pfizer <i>New York, NY</i>	for active immunization to prevent invasive streptococcal pneumonia	3/31/2009	2/24/2010	7.8 months
<i>For more information, contact: Pfizer at (800) 879-3477 or www.prevnar13.com</i>					
Provenge® sipuleucel-T (P)	Dendreon <i>Seattle, WA</i>	treatment of metastatic hormone-refractory prostate cancer	10/30/2009	4/29/2010	6.0 months
<i>For more information, contact: Dendreon at (877) 256-4545 or www.provenge.com</i>					

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.

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A Look at the New Drugs and Biologics Approved in 2010

Twenty-six 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 2010. 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.

ALLERGY

Lastacaft™ (alcaftadine ophthalmic solution) was approved for the prevention of itching associated with allergic conjunctivitis in patients over age 2. Lastacaft is an H1 histamine receptor antagonist that inhibits the release of histamine from cells. Lastacaft was developed by Vistakon Pharmaceuticals, LLC and marketed by Allergan, Inc. in the United States.

ARTHRITIS/MUSCULOSKELETAL

Actemra® (tocilizumab) is the first interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody approved to treat rheumatoid arthritis (RA). It was approved for the treatment of adults with moderate to severe active rheumatoid arthritis who have had an inadequate response to other approved RA medicines. Actemra works by inhibiting the activity of IL-6, an immune system protein involved in the inflammatory process and is elevated in patients with RA. It has shown to relieve both inflammation of the joints and certain systemic symptoms of RA. RA is a chronic, progressive inflammatory disease affecting the joints and surrounding tissues, causing intense pain, irreversible joint destruction and systemic complications. The Arthritis Foundation estimates that 1.3 million Americans suffer from RA. Actemra was developed by Genentech, Inc., a wholly-owned member of the Roche Group.

Krystexxa™ (pegloticase) was approved for the treatment of chronic gout in adults who are refractory to conventional therapy. It is the first and only treatment approved by the FDA for adults with refractory chronic gout. Gout is a painful condition due to an excess of bodily waste uric acid, eventually deposited as needle-like crystals in the joints and soft tissue. It is estimated that 3 percent of the 3 million adults who suffer from gout are not helped by conventional therapy. Krystexxa is a PEGylated uric acid-specific enzyme that lowers uric acid levels by metabolizing it into a harmless chemical that is excreted in the urine. In clin-

ical trials, patients treated with Krystexxa experienced significant clinical improvement within six months of therapy. Krystexxa was developed by Savient Pharmaceuticals, Inc.

Prolia™ (denosumab), the first approved RANK ligand inhibitor, is indicated for the treatment of postmenopausal women with osteoporosis at high-risk for fracture. It is given by injection every six months. In clinical trials, it reduced the risk of fracture at the spine, hip, and other sites. Prolia specifically targets RANK ligand, an essential regulator of osteoclasts (the cells that break down bone). One in two women in the United States over the age of 50 with postmenopausal osteoporosis will experience a fracture in her remaining lifetime. In clinical trials, Prolia demonstrated a 68 percent reduction in vertebral fractures, a 40 percent reduction in hip fractures, a 20 percent reduction in non-vertebral fractures and significant bone density increases at key sites. Prolia was discovered and developed by Amgen Inc.

Xiaflex™ (collagenase clostridium histolyticum) is a first-in-class medicine approved to treat Dupuytren's contracture, a progressive hand disease. Before the approval of Xiaflex, the only effective treatment was hand surgery. Dupuytren's occurs when too much collagen builds up, forming thick, rope-like cords of tissue that prevent the fingers from relaxing and straightening normally. Xiaflex is made from a protein and works by breaking down the excessive buildup of collagen (the cord) in the hand via injection directly into the cord. Xiaflex was developed by Auxilium Pharmaceuticals, Inc.

CANCER

Halaven™ (eribulin) was approved for the treatment of metastatic breast cancer in patients who have previously received at least two chemotherapy treatments for metastatic disease. Halaven is a non-taxane, microtubule dynamics inhibitor that is a synthetic analogue of halichondrin B, a product isolated from the marine sponge *Halichondria okadai*. It is believed to work by inhibiting cancer cell growth. In clinical trials, patients treated with Halaven survived a median of 2.4 months longer than those treated with a single-agent treatment. Breast cancer is the second leading cause of cancer-related death in women, according to the National Cancer Institute. More than 200,000 women will be diagnosed with breast cancer this year and more than 40,000 will die from the disease. It is estimated that

10 percent of women with breast cancer will have metastatic disease at the time of diagnosis and an estimated 20 percent of early-stage breast cancer will go on to develop metastatic disease within five years. Halaven was developed by Eisai Inc.

Jevtana[®] (cabazitaxel) was approved for the intravenous treatment, in combination with prednisone, of hormone-refractory metastatic prostate cancer previously treated with a docetaxel containing treatment. In prostate cancer, testosterone can cause prostate tumors to grow. Treatments are used to reduce or block testosterone production, but in hormone refractory disease, cancer cells continue to grow despite testosterone suppression. In clinical studies, Jevtana demonstrated statistically significant survival benefit in second-line treatment. Jevtana was developed by sanofi-aventis.

Provenge[®] (sipuleucel-T) was approved for the treatment of asymptomatic or minimally symptomatic metastatic, castrate-resistant (hormone-refractory) prostate cancer. Provenge is the first in a new therapeutic class known as autologous cellular immunotherapy. It is designed to induce an immune response against prostatic acid phosphatase (PAP), an antigen expressed in most prostate cancers. Each dose of Provenge is manufactured using the patient's own immune cells from the blood. To enhance their therapeutic response against the cancer, the immune cells are then exposed to the PAP antigen and then linked to an immune stimulating substance. When this process is complete, the patient's cells are returned intravenously to the patient to treat the cancer. Provenge was developed by Dendreon Corporation.

CONTRACEPTION

ella[®] (ulipristal acetate) was approved as a prescription-only emergency contraceptive indicated for use within 120 hours (five days) of unprotected intercourse or a known or suspected contraceptive failure. Ella is a progesterone agonist/antagonist that potentially inhibits follicular rupture when taken just before ovulation is to occur. Ella was developed by HRA Pharma of France and will be marketed by Watson Pharmaceuticals, Inc. in the United States.

Natazia[®] (estradiol valerate/estradiol valerate dienogest) is the first in a new class of oral contraceptives to deliver estradiol. Natazia combines two female hormones—an estrogen and a progestin—and is the first four-phasic oral contraceptive in the United States. Four-phasic refers to the doses of progestin and estrogen varying at four times throughout each 28-day treatment cycle. It delivers varying doses of estradiol valerate and the combination of estradiol valerate and dienogest on different days of the cycle. Natazia was developed by Bayer HealthCare Pharmaceuticals Inc.

DIABETES

Victoza[®] (liraglutide [rDNA origin] injection) is the first glucagon-like peptide-1 (GLP-1) analogue developed for the treatment of type 2 diabetes. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. In type 2 diabetes, patients cannot make and use insulin, causing a buildup of sugar (glucose) in the blood. Victoza works by stimulating the release of insulin from the pancreatic beta cells only when blood sugar levels are high. Victoza was developed by Novo Nordisk Inc.

GENETIC DISORDERS

Carbaglu[®] (carglumic acid) was approved to treat a rare, genetic disorder that results in too much ammonia in the blood. NAGS deficiency (N-acetylglutamate synthase) is extremely rare and can be present in babies soon after birth. Carbaglu was approved to treat pediatric and adult patients with acute hyperammonemia due to a deficiency of hepatic enzyme N-acetylglutamate synthase and as maintenance therapy for chronic hyperammonemia due to NAGS deficiency. Carbaglu was developed by Orphan Europe, headquartered in Paris, France and part of the Recordati Group in Italy.

Glassia[™] (alpha-1-proteinase inhibitor), the first and only liquid alpha-1-proteinase inhibitor, was approved for the treatment of alpha-1 deficiency (AATD). It is indicated for chronic augmentation and maintenance therapy in adults with emphysema due to congenital deficiency of alpha-1-proteinase inhibitor. Glassia was developed by Kamada in Israel and marketed by Baxter International in the United States.

Hizentra[™] (immune globulin subcutaneous, human) is a once-weekly replacement therapy approved for the treatment of primary immunodeficiency (PI). Primary immunodeficiencies are comprised of a group of disorders, usually genetic, that cause a malfunction in all or part of the immune system, leaving the patient unable to fight off infections caused by everyday germs. There are nearly 100 types of PIs affecting an estimated 10 million people worldwide. Hizentra is the first 20 percent subcutaneous immune globulin approved in the United States. The high concentration globulin is stabilized by a naturally occurring amino acid that allows the product to be stored at room temperature, making it ready to use, offering convenience and portability. Hizentra was developed by CSL Behring.

Lumizyme[®] (alglucosidase alfa for injection) was approved for the treatment of late-onset (non-infantile) Pompe disease in patients ages 8 years and older. Pompe disease is a rare genetic disorder. Primary symptoms include heart and skeletal muscle weakness, progressing to respiratory weakness and death from respiratory failure. In Pompe disease, a gene mutation

prevents the body from making an enzyme called acid alpha-glucosidase (GAA), which is necessary for proper muscle function. GAA is used by the heart and muscle cells to convert a sugar called glycogen into energy. Without the enzyme action, glycogen builds up in the cells and weakens the heart and muscles. Lumizyme is believed to work by replacing the deficient GAA, thereby reducing the accumulated glycogen in the heart and skeletal muscle cells. Lumizyme was developed by Genzyme Corporation.

Vpriv[®] (velaglucerase alfa), a human cell-line-derived enzyme replacement therapy, was approved for the long-term treatment of type 1 Gaucher disease in children and adults. Gaucher disease is a rare genetic disorder where a gene mutation causes patients to not produce enough of an enzyme called glucocerebrosidase. Without this enzyme, harmful amounts of a certain lipid can build up in the liver, spleen, bones, bone marrow and nervous system and can prevent cells and organs from working properly. Only about 1 in 50,000 to 1 in 100,000 people have Gaucher disease. Vpriv is approved for type 1 Gaucher disease, the most common form of the disorder. Vpriv was developed by Shire Human Genetic Therapies, Inc.

INFECTIOUS DISEASES

Menveo[®] (meningococcal [groups A, C, Y and W-135] oligosaccharide diphtheria¹⁹⁷ conjugate vaccine) is a quadrivalent meningococcal conjugate vaccine approved for the active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135 in people ages 11 to 55. Meningococcal disease infects about 1,000 to 3,000 people each year in the United States. It is the leading cause of bacterial meningitis, which is an infection around the brain and spinal cord, and sepsis, an often life-threatening bloodstream infection. Menveo was developed by Novartis Vaccines & Diagnostics, Inc.

Pprevnar 13[™] (pneumococcal 13-valent conjugate vaccine [diphtheria CRM¹⁹⁷ protein]) is a vaccine approved for the active immunization of children ages 6 weeks through 5 years for the prevention of invasive disease and otitis media (middle ear infection) caused by *Streptococcus pneumoniae*. Invasive pneumococcal disease includes sepsis and bacteremia, meningitis, bacteremic pneumonia, and empyema. Pprevnar 13 extends protection to 13 different serotypes of *Streptococcus pneumoniae* and is a successor to Pprevnar, which was approved in 2000. The original vaccine protected against seven serotypes of the bacterium. The bacterium can cause infections of the blood, middle ear, the covering of the brain and spinal cord, and pneumonia. Currently, 62 percent of invasive pneumococcal disease is caused by the six additional serotypes included in Pprevnar 13. Pprevnar

was developed by Pfizer Inc. and its wholly-owned subsidiary Wyeth Pharmaceuticals Inc.

Teflaro[™] (ceftaroline fosamil) is a broad-spectrum cephalosporin antibiotic with activity against both gram-positive and gram-negative microorganisms. It is indicated for the treatment of community-acquired bacterial pneumonia (CABP), including infections caused by *Streptococcus pneumoniae* bacterium, and acute bacterial skin and skin structure infection (ABSSI), including infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA).

Cephalosporins, the most prescribed class of antibiotics in the world, act by interfering with the bacterial cell wall. Teflaro was developed by Cerexa (a wholly-owned subsidiary of Forest Laboratories) and will be marketed in the United States by Forest Laboratories, Inc.

MENTAL ILLNESSES

Latuda[®] (lurasidone) is a once-daily atypical antipsychotic approved for the treatment of schizophrenia, a chronic brain disorder that affects about 2.4 million American adults. It is characterized by symptoms such as hallucination, delusion, disorganized thinking, lack of emotion and energy, as well as problems with memory, attention and the ability to plan, organize and make decisions. In clinical trials, Latuda demonstrated significantly greater improvement over placebo on the Positive and Negative Syndrome Scale (PANSS) and the Brief Psychiatric Rating Scale derived from PANSS. Latuda was developed by Sunovion Pharmaceuticals Inc.

NEUROLOGICAL DISORDERS

Ampyra[®] (dalfampridine) is the first FDA-approved therapy for walking impairment associated with multiple sclerosis (MS), a chronic, often disabling disease that affects the central nervous system—the brain, spinal cord, and optic nerves. More than 400,000 Americans have MS, and research indicates that between 64 percent and 85 percent of those have difficulty walking, and 70 percent who have difficulty walking report it to be the most challenging aspect of their disease. In the laboratory, Ampyra was found to improve muscle conduction in nerve fibers in which the insulating layer, called myelin, has been damaged. In clinical trials, Ampyra demonstrated an increase in walking speeds in all four major types of MS—relapsing-remitting, secondary progressive, progressive relapsing, and primary progressive. Ampyra was developed by Acorda Therapeutics, Inc.

Gilenya[™] (fingolimod) is the first oral medicine approved for the treatment of relapsing forms of multiple sclerosis (MS). Gilenya is the first in a new class of drugs called sphingosine 1-phosphate receptor (S1PR) modulators. In MS, the immune system damages the

covering that protects nerve fibers in the central nervous system. Gilenya is thought to work by retaining certain white blood cells (lymphocytes) in the lymph nodes. This prevents the lymphocytes from reaching the central nervous system, where they could potentially attack the protective covering around the nerve fibers, resulting in less inflammatory damage to the nerve cells. In clinical trials, it reduced relapses by 52 percent after one year of treatment compared to interferon beta-1a (a commonly prescribed treatment). Gilenya was developed by Novartis Pharmaceuticals Corporation.

Xeomin[®] (incobotulinumtoxinA) is a botulinum toxin type A for the treatment of adults with cervical dystonia or blepharospasm. Dystonias are neurological movement disorders where sustained muscle contractions cause twisting and repetitive movements or abnormal postures. These involuntary and painful movements can affect a single muscle (focal), a group of muscles such as those in the arms, legs or neck (segmental), or even the entire body (generalized). Cervical dystonia and blepharospasm are focal types of dystonias. A proprietary manufacturing process isolates the therapeutic component of toxin and eliminates accessory proteins. Xeomin was developed by Merz Pharmaceuticals, LLC.

STROKE

Pradaxa[®] (dabigatran etexilate) was approved to reduce the risk of stroke and systemic embolism in patients with atrial fibrillation. It is the first anticoagulant approved in the United States in more than 50 years. Atrial fibrillation (abnormal heart rhythm) can cause blood clots to form in the heart that can travel to the brain causing a stroke. An estimated 2.3 million Americans are living with atrial fibrillation. Pradaxa is an anticoagulant that inhibits thrombin, an enzyme in the blood that is involved in blood clotting. In clinical

trials, patients taking Pradaxa had fewer strokes (both ischemic and hemorrhagic) than those taking warfarin. Treatment with Pradaxa does not require blood monitoring or related dose adjustments like warfarin. Pradaxa was discovered and developed by Boehringer Ingelheim Pharmaceuticals, Inc.

OTHER DISEASES

Asclera[®] (polidocanol) was approved to treat small varicose veins (abnormally swollen or twisted veins). Asclera, an injectable, is used in a procedure called sclerotherapy and is administered by a healthcare provider to treat two types of veins—uncomplicated spider veins (≤ 1 mm in diameter) and uncomplicated reticular veins (1mm to 3 mm in diameter). Asclera works by damaging the cell lining of blood vessels, causing them to close and eventually to be replaced by other types of tissue. Asclera was developed by Chemische Fabrik Kreussler & Co. GmbH of Germany and will be marketed by Merz Aesthetics, Inc. in the United States.

Egrifta[™] (tesamorelin for injection) is the first and only treatment for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy. Several factors, including antiretroviral therapy and the HIV virus itself are thought to contribute to HIV-associated lipodystrophy, which causes changes to body composition and can include excess abdominal fat accumulation. In clinical trials, Egrifta demonstrated the reduction in visceral adipose tissue and waist circumference. Egrifta is a synthetic analogue of the human growth hormone-releasing factor (GRF) that acts on the pituitary cells in the brain to stimulate the synthesis and release of endogenous growth hormone. Egrifta was developed by Theratechnologies Inc. of Canada and will be marketed in the United States by EMD Serono.

allergic conjunctivitis—Inflammation of the tissue lining the eyelids (conjunctiva) due to a reaction from allergy-causing substances such as pollen and dander.

alpha-1 proteinase inhibitor deficiency—Also called alpha-1 antitrypsin deficiency, which is an inherited disorder that may cause lung and liver diseases. People with alpha-1 antitrypsin deficiency usually develop the first signs and symptoms of lung disease between the ages of 20 and 50. The earliest symptoms are shortness of breath following mild activity, reduced ability to exercise, and wheezing. Other signs and symptoms can include unintentional weight loss, recurring respiratory infections, fatigue, and rapid heartbeat upon standing. Affected individuals often develop emphysema, which is a lung disease caused by damage to the small air sacs in the lungs (alveoli).

atrial fibrillation/flutter—Very fast electrical discharge patterns that make the heart's atria contract extremely rapidly, which causes the ventricles to contract faster and less efficiently than normal. As a result, inadequate amounts of blood are pumped out of the heart, blood pressure falls, and heart failure may occur.

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

blepharospasm—Eyelid twitching, which is usually caused by fatigue, stress, and caffeine.

breast cancer—A malignant tumor that has developed from cells in the breast. It is the most common form of cancer in women and is the second-leading cause of cancer death in women, exceeded only by lung cancer.

cervical dystonia—Disorder or lack of tone in the muscles of the neck.

diabetes, type 2—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. 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.

Dupuytren's disease—An abnormal thickening of the tissue just beneath the skin known as fascia. The thickening occurs in the palm and can extend into the fingers. Firm cords and lumps may develop that can cause the fingers to bend into the palm, in which case it is described as Dupuytren's contracture. Although the skin may become involved in the process, the deeper structures—such as the tendons—are not directly involved. Occasionally, the disease will cause thickening on top of the finger knuckles (knuckle pads) or nodules or cords within the soles of the feet (plantar fibromatosis).

Gaucher disease—An inherited disease caused by a lack or deficiency of an enzyme (glucocerebrosidase). It primarily affects the liver, spleen and bone marrow, usually resulting in death.

gout—The pain of gout (called attacks or flares) is caused by inflammation when needle-like crystals are deposited in connective tissue and/or in the fluid that cushions a joint (the synovial fluid). These crystals are made up of uric acid, a substance produced when the body breaks down purines found in human tissue and many foods we eat. Most uric acid is carried through the bloodstream to the kidneys, which eliminate it from the body in the urine. However, if the body produces

too much uric acid or if the kidneys don't eliminate enough of it, uric acid can build up in the blood. An attack usually starts with sudden, severe pain, tenderness, redness, warmth, and swelling in the large joint of the big toe. Other joints may include the instep, ankles, heels, knees, wrists, fingers, and elbows. Rarely, the shoulders, hips, or spine may be affected. After about 3-10 days, the attack usually subsides, and the next one may not happen for months or even years. But over time, the gout attacks can become more severe, last longer, affect more than one joint, and occur more often.

meningococcal disease—Describes infections caused by the bacterium *Neisseria meningitidis* (also termed meningococcus). It carries a high mortality rate if untreated. While it is best known as a cause of meningitis, it also causes widespread blood infection (sepsis), which is more damaging and dangerous. Meningitis and meningococcal sepsis are major causes of illness, death, and disability in both developed and underdeveloped countries worldwide.

multiple sclerosis (MS)—Progressive disease of the central nervous system in which scattered patches of the covering of nerve fibers (myelin) in the brain and spinal cord are destroyed. Symptoms range from numbness and tingling to paralysis and incontinence.

NAGS (N-acetylglutamate synthase) deficiency—A condition that results in too much ammonia in the blood. NAGS deficiency is an extremely rare, genetic disorder that can be present in babies soon after birth. NAGS deficiency and the resulting elevated levels of ammonia (hyperammonemia) can be fatal if not detected and treated rapidly. DNA testing can confirm the diagnosis of NAGS.

GLOSSARY

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

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.

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.

osteoporosis—The most common metabolic bone disease in older people. It may be associated with other diseases such as rheumatoid arthritis or with the use of medications such as corticosteroids. A reduction in bone mass leads to fractures, especially of the vertebrae, hips and wrists.

Pompe disease—A rare (estimated at 1 in every 40,000 births), inherited and often fatal disorder that disables the heart and muscles. It is caused by mutations in a gene that makes an enzyme called alpha-glucosidase (GAA). Normally, the body uses GAA to break down

glycogen, a stored form of sugar used for energy. But in Pompe disease, mutations in the GAA gene reduce or completely eliminate this essential enzyme. Excessive amounts of glycogen accumulate everywhere in the body, but the cells of the heart and skeletal muscles are the most seriously affected. The symptoms of Pompe disease can vary widely in terms of age of onset and severity depending on the degree of enzyme deficiency.

primary immunodeficiency disease (PID)—An inherited disorder that affects some 50,000 people in the United States. The disorder requires regular immunoglobulin replacement therapy to prevent potentially serious or life-threatening infections.

prostate cancer—An uncontrolled (malignant) growth of cells in the prostate gland that is located at the base of the urinary bladder and is responsible for helping control urination as well as forming part of the semen. Prostate cancer is the second leading cause of death of males in the United States.

rheumatoid arthritis—A type of arthritis that particularly attacks the small joints of the hands, wrists and feet. With this autoimmune disorder, the joints become painful, swollen, stiff and, in severe cases, deformed.

schizophrenia—The most common form of psychotic illness charac-

terized by disturbances in thinking, emotional reaction and behavior. It is disabling and has a prolonged course that almost always results in chronic ill health and some degree of personality change.

streptococcal infections—Also called “strep,” which can cause a variety of health problems. There are two types: group A and group B. Antibiotics are used to treat both. Group A strep causes strep throat, scarlet fever, impetigo, toxic shock syndrome, and cellulitis and necrotizing fasciitis (the flesh-eating disease). Group B strep can cause blood infections, pneumonia and meningitis in newborns. Adults can also get group B strep infections, especially if they are elderly or already have health problems. Strep B can cause urinary tract infections, blood infections, skin infections and pneumonia in adults.

varicose veins—Swollen, twisted, and sometimes painful veins that have filled with an abnormal collection of blood. In normal veins, valves in the vein keep blood moving forward toward the heart. With varicose veins, the valves do not function properly, allowing blood to remain in the vein. Pooling of blood in a vein causes it to enlarge. That process usually occurs in the veins of the legs, although it may occur elsewhere. Varicose veins are common, affecting mostly women.

THE DRUG DISCOVERY, DEVELOPMENT AND APPROVAL PROCESS

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.

Discovery/ Preclinical Testing		Clinical Trials			FDA	Phase IV
Years	6.5	Phase I	Phase II	Phase III	1.5	
Test Population	Laboratory and animal studies	20 to 100 healthy volunteers	100 to 500 patient volunteers	1,000 to 5,000 patient volunteers	Review process/ approval	Additional post-marketing testing required by FDA
Purpose	Assess safety, biological activity and formulations	Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use		
Success Rate	5,000 compounds evaluated	5 enter trials			1 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 lab to U.S. patients, according to the Tufts Center for the Study of Drug Development, based on drugs approved from 1994 through 1998. 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 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 normal, 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. The average review time for the 21 new therapeutics approved by the FDA in 2010 was 14.8 months.

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. Pharmaceutical companies invested an estimated \$67.4 billion in research and development in 2010.

R&D Investment by U.S. Biopharmaceutical Companies Remained Strong in 2010

Demonstrating a steady and ongoing commitment to innovative R&D, America's biopharmaceutical research companies invested a record \$67.4 billion last year in the research and development of new medicines and vaccines—an increase of \$1.5 billion from 2009, according to analyses by the Pharmaceutical Research and Manufacturers of America (PhRMA) and Burrill & Company.

PhRMA member companies alone spent an estimated \$49.4 billion on biopharmaceutical R&D last year, a 6.4 percent increase over 2009, according to the PhRMA survey. The Burrill & Company analysis shows that additional biopharmaceutical research companies in the United States spent an estimated \$18.0 billion on R&D in 2010.

America's biopharmaceutical research companies lead the world in the pursuit of new, life-saving and life-enhancing medicines.

The percentage of U.S. sales that PhRMA member companies invested in R&D also grew. Over the past decade, biopharmaceutical companies have consistently invested around 19 percent of domestic sales on R&D activities; in 2010, that figure jumped to 20.5 percent. This echoes previous findings about sector commitment to R&D, such as that of the nonpartisan Congressional Budget Office (CBO), which called the sector "one of the most research-intensive industries in the United States."

"America's biopharmaceutical research companies encounter significant challenges throughout the

DOMESTIC R&D AND R&D ABROAD,
PhRMA MEMBER COMPANIES: 1970-2010**

Year	Domestic R&D	Annual Percentage Change	R&D Abroad	Annual Percentage Change	Total R&D	Annual Percentage Change
*2010	\$37.4 B	5.7%	\$12.0 B	8.7%	\$49.4 B	6.4%
2009	35.4	-0.6	11.1	-6.1	46.4	-2.0
2008	35.6	-2.8	11.8	4.6	47.4	-1.1
2007	36.6	7.8	11.3	25.4	47.9	11.5
2006	34.0	9.7	9.0	1.3	43.0	7.8
2005	31.0	4.8	8.9	19.1	39.9	7.7
2004	29.6	9.2	7.5	1.0	37.0	7.4
2003	27.1	5.5	7.4	37.9	34.5	11.1
2002	25.7	9.2	5.4	-13.9	31.0	4.2
2001	23.5	10.0	6.2	33.3	29.8	14.4
2000	21.4	15.7	4.7	10.6	26.0	14.7
1999	18.5	7.4	4.2	9.9	22.7	8.2
1998	17.1	11.0	3.8	9.9	21.0	10.8
1997	15.5	13.9	3.5	6.5	19.0	12.4
1996	13.6	14.8	3.3	-1.6	16.9	11.2
1995	11.9	7.0	3.3	***	15.2	***
1990	6.8	13.0	1.6	23.6	8.4	14.9
1985	3.4	13.3	0.7	17.2	4.1	13.9
1980	1.5	16.7	0.4	42.8	2.0	21.5
1975	0.9	13.9	0.2	7.0	1.1	12.8
1970	0.6	—	0.05	—	0.6	—

* 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.

Source: Pharmaceutical Research and Manufacturers of America, *PhRMA Annual Membership Survey, 2011*.

research and development process, but still they do not falter in their commitment,” said PhRMA President and CEO John J. Castellani. “This dedication to innovation means hope for millions of American patients and value for the healthcare system as a whole. Improved treatment options can lead to better patient health and to controlled healthcare costs in the future.”

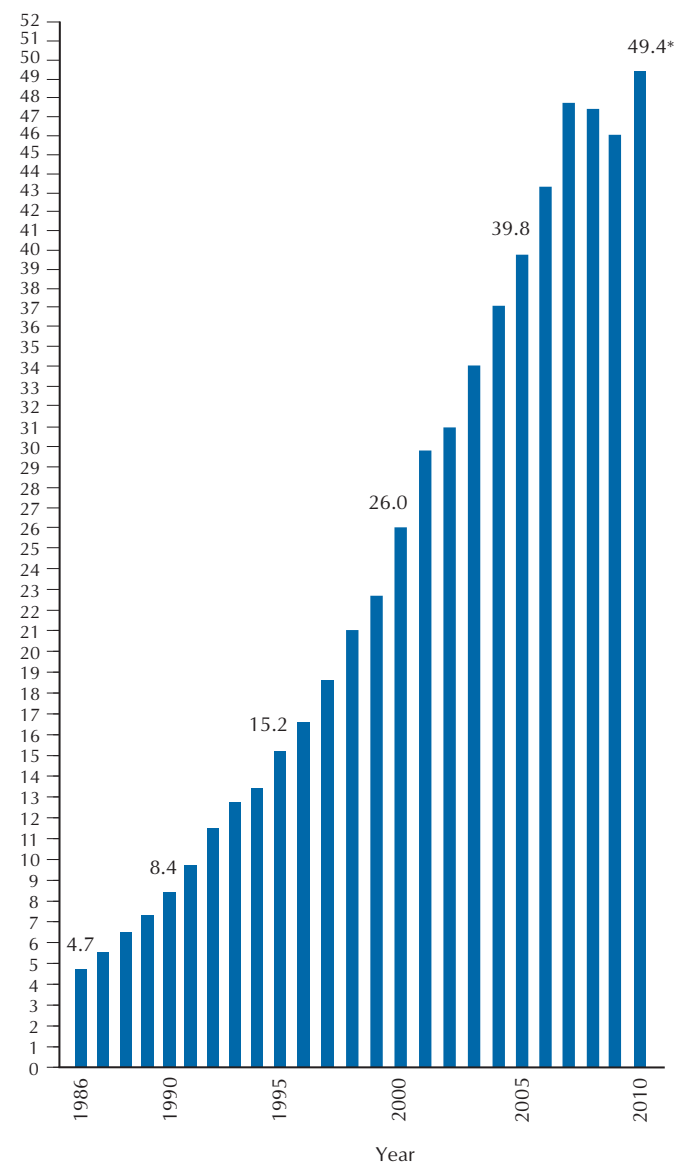
U.S.-based biopharmaceutical research does not just lead to tomorrow’s new medicines—it also supports jobs today. According to a recent study conducted by Archstone Consulting, roughly 655,000 people in the United States worked for America’s biopharmaceutical

research companies in 2008 (the most comprehensive analysis). Importantly, each of those jobs supported 3.7 additional jobs, with a total of nearly 3.1 million jobs supported by the sector.

One way that biopharmaceutical research companies support additional jobs is through the collaborative research ecosystem that helps America maintain its place as the global leader in worldwide medical innovation. By building on the basic research conducted by government-funded academic researchers, biopharmaceutical companies help to spur continued research at all levels.

R&D INVESTMENTS BY PhRMA MEMBER COMPANIES, 1986-2010

Expenditures (\$ billions)



*Estimated

Source: Pharmaceutical Research and Manufacturers of America, *PhRMA Annual Membership Survey, 2011*

R&D AS A PERCENTAGE OF SALES, PhRMA MEMBER COMPANIES: 1970-2010

Year	Domestic R&D as a % of Domestic Sales	Total R&D as a % of Total Sales
*2010	20.5%	17.0%
2009	19.5%	16.8%
2008	19.4%	16.6%
2007	19.8%	17.5%
2006	19.4%	17.1%
2005	18.6%	16.9%
2004	18.4%	16.1%**
2003	18.3%	16.5%**
2002	18.4%	16.1%
2001	18.0%	16.7%
2000	18.4%	16.2%
1999	18.2%	15.5%
1998	21.1%	16.8%
1997	21.6%	17.1%
1996	21.0%	16.6%
1995	20.8%	16.7%
1990	17.7%	14.4%
1985	16.3%	12.9%
1980	13.1%	8.9%
1975	12.7%	9.0%
1970	12.4%	9.3%

* Estimated

** Revised in 2007 to reflect updated data.

Source: Pharmaceutical Research and Manufacturers of America, *PhRMA Annual Membership Survey, 2011*



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