MEDICINES IN DEVELOPMENT

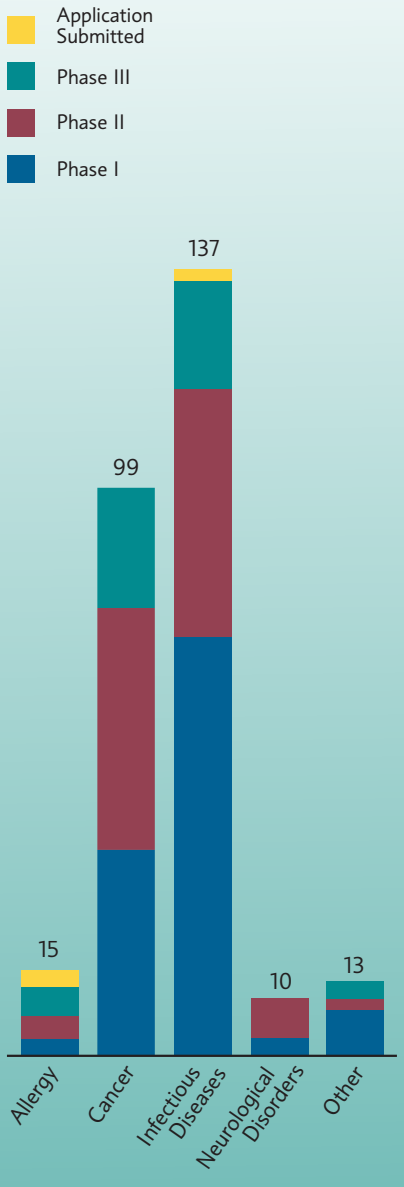
Vaccines

A Report on the Prevention and Treatment of Disease Through Vaccines

PRESENTED BY AMERICA'S BIOPHARMACEUTICAL RESEARCH COMPANIES

2013 REPORT

Vaccines in Development*



*Some vaccines are listed in more than one category.

Nearly 300 Vaccines Are in Development; Research Focuses on Prevention and Treatment

For many years, vaccines have been used to successfully prevent devastating infectious diseases such as smallpox, measles and polio. According to data from the U.S. Centers for Disease Control and Prevention (CDC), 10 infectious diseases have been at least 90 percent eradicated in the United States thanks to vaccines. This has protected millions of children and families from needless illness.

These public health triumphs illustrate the major contributions that vaccines have made in saving countless lives around the world. In the past several years, through our growing understanding of the molecular underpinnings of disease and technological advances, many new vaccines have been developed, including one against human papillomavirus (HPV) infections that can lead to cervical cancer, a vaccine to guard against the anthrax virus before exposure, and a vaccine to prevent pneumococcal infections in high-risk populations.

But vaccines are not only for preventing infectious diseases, some help the body fight a range of illnesses by activating the immune system to recognize and attack disease. In 2010, a new cancer vaccine for the treatment of prostate cancer was approved in the United States, and many more immunotherapeutic vaccines are in development.

Today, biopharmaceutical research companies are developing 271 vaccines for infectious diseases, cancer, neurological disorders, allergies and other diseases. Among the projects in development are:

- A therapeutic vaccine for **HIV infection** intended to delay disease progression.
- A monoclonal antibody vaccine that targets both pandemic and seasonal **influenza**.
- A genetically-modified vaccine designed for the treatment of **pancreatic cancer**.
- An irradiated vaccine for protection against **malaria**.

The development and regulatory path that these vaccine candidates face is complex. As with the development of all drugs, the majority of vaccines must prevail through years of clinical testing before they can be approved for use by the general public. However, advances in other scientific fields, such as genomics and manufacturing technologies, are becoming increasingly useful in the development of new vaccines. The continued efforts of researchers within biopharmaceutical companies and across the ecosystem, who are pursuing new techniques and strategies in vaccine development, create tremendous opportunities to protect against many more life-threatening diseases in the future.

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RESEARCH • PROGRESS • HOPE

Innovative Vaccines in the Pipeline

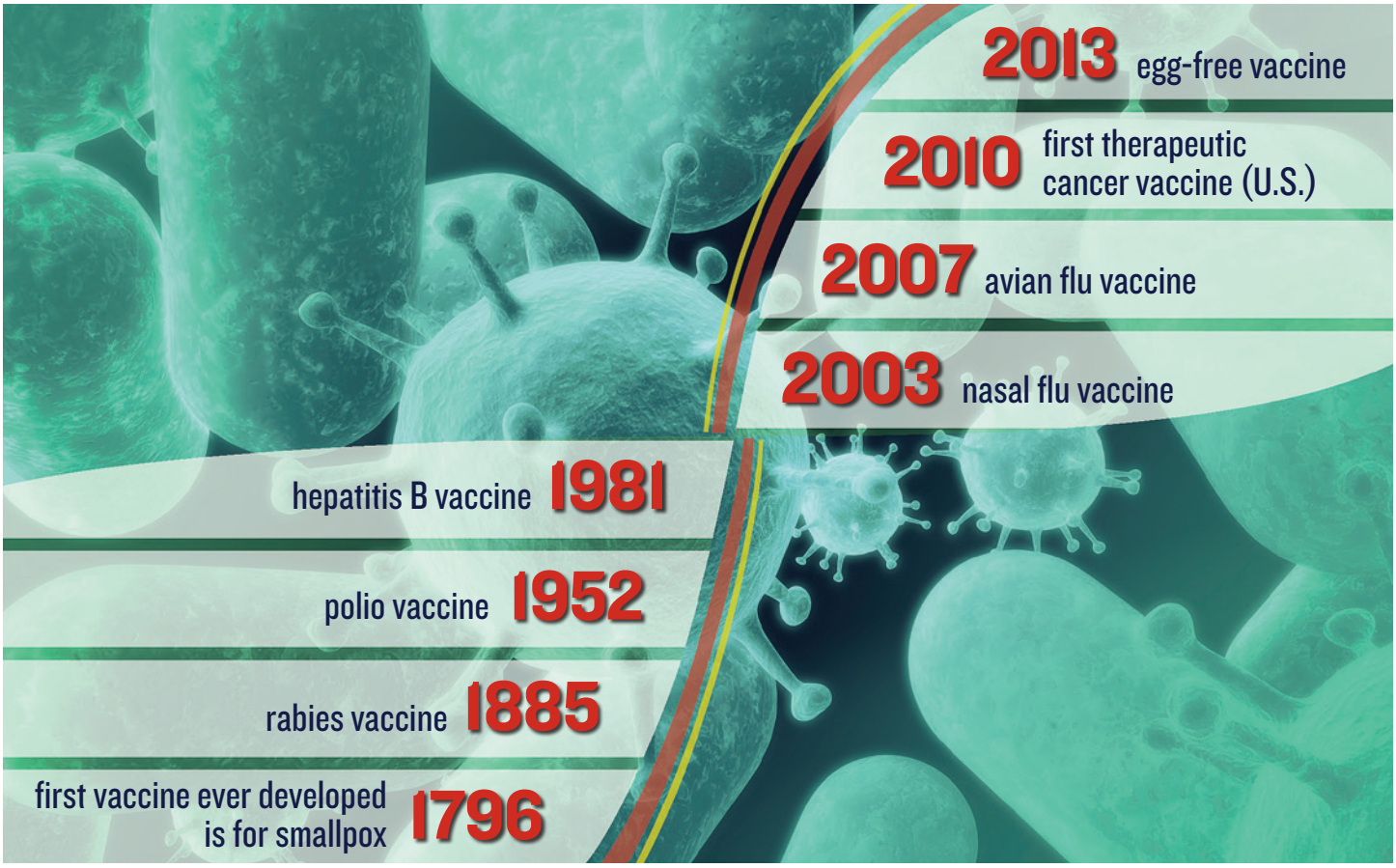
Building on the transformational successes to date, the future of vaccines—both for the prevention and treatment of disease—offers great hope for improving and preserving public health in the United States and across the globe. The 271 medicines in development span a wide array of diseases, and employ exciting new scientific and technical knowledge. Here are a few examples of the promising vaccines in the pipeline:

Malaria—A malaria vaccine in development has shown to be 100 percent effective in early clinical trials in preventing the transmission of the disease from infected mosquitoes to humans. The vaccine builds on initial knowledge gained in the 1970s, where researchers demonstrated that long-term protection against malaria was possible when volunteers received thousands of bites from radiated infected mosquitoes. The vaccine in development uses a weakened form of the whole sporozoite, a life-stage of the parasite *Plasmodium falciparum* that causes malaria. This weakened form of the parasite is enough to cause an immune response, but not cause the disease, thus leading to protection against any future malarial bite infection.

Cervical Cancer—A live, attenuated *Listeria* monocytogenes (LM)-based immunotherapy is in development for the treatment of women who already have cervical cancer as a result of infection by the human papillomavirus (HPV). The vaccine targets the HPV gene E7, which is responsible for the transformation of HPV-infected cells into dysplastic or malignant tissue. The vaccine is engineered to secrete a fusion protein that instructs the body's immune system to destroy the tumors.

HIV Infection—A therapeutic vaccine in development is targeting the low-mutating (conserved) parts from the protein p24 of the HIV virus. The vaccine consists of four peptides that are modified to increase the immune response against the conserved parts of the p24 protein. A sustained immune response against the p24 protein has shown to be associated with delayed disease progression.

Milestones in Vaccine Development



Influenza—A monoclonal antibody (mAb) vaccine in development targets both pandemic and severe seasonal influenza A virus infections. The mAb vaccine, made from recombinant human antibodies from human B-cell cultures, specifically targets the M2 protein of the virus, which is essential for the influenza virus to function normally.

Pancreatic Cancer–A potential treatment for pancreatic cancer is a combination of two therapeutic vaccines. The treatment combines a *Listeria*-based vaccine that has been engineered to express the tumor-associated antigen mesothelin and allogeneic pancreatic cancer cells that are genetically-modified to secrete the immune-stimulant, granulocyte-macrophage colony stimulating factor (GM-CSF). The cells are irradiated to prevent further cell growth although they stay metabolically active. Sequential administration of the vaccines in animal studies have demonstrated enhanced tumor-specific T-cell and anti-tumor responses.

Smoking Cessation–One in a new class of targeted vaccines in development induces an antigen-specific immune activation for smoking cessation and relapse prevention. It is made from biocompatible and biodegradable materials and is a fully synthetic nanoparticle vaccine engineered to mimic the properties of natural pathogens to elicit an immune response.

"More than two-thirds of new vaccines developed in the last 25 years have been developed from the United States."

Source: *PhRMA 2013 Vaccine Fact Book*

Preventative Vaccines: Positive Impact to Health and Society

Vaccines are one of the most profound achievements of biomedical science and public health. Spanning more than 200 years of research and development, 10 infectious diseases have been at least 90 percent eradicated in the United States thanks to vaccines. This has protected millions of children and families from avoidable illness.

The prevention of disease has an enormous impact on the health of individuals, but also the health of communities and

RESEARCH & HOPE AWARDS

On September 11, 2013, PhRMA, along with distinguished members of the medical, patient, and provider communities, presented the second annual Research & Hope Awards. This year's program highlighted the history, progress and promising future of vaccines and immunization. PhRMA proudly presented the following awards:

The Research & Hope Award for Academic or Public Research in Vaccine Development
Presented to individuals or a team from academic or government institutions for outstanding research in the area of vaccine development.
2013 award presented to: **Douglas R. Lowy, M.D., and John T. Schiller, Ph.D., National Cancer Institute**

The Research & Hope Award for Biopharmaceutical Industry Research in Vaccine Development
Presented to individuals or team from a biopharmaceutical company for outstanding research in the area of vaccine development.
2013 award presented to: **GlaxoSmithKline Malaria Vaccine Team**

The Research & Hope Award for Patient and Community Health
Presented to an individual or organization that has had a significant impact educating parents, health care providers or students about the importance of childhood immunizations and facilitating increased vaccinations in their community.
2013 award presented to: **Linda Y. Fu, M.D., Children's National Medical Center**

To learn more about the dedicated researchers honored with the 2013 Research & Hope Awards, please visit www.phrma.org/awards.

economies by reducing health care costs and avoiding lost productivity. Preventative vaccines are given to individuals, but see their greatest benefit when entire populations are immunized. When a high level of vaccination is achieved in a community with an effective vaccine, disease transmission can be successfully interrupted. When disease transmission is interrupted, even those who did not receive the vaccine, or those who did not receive immunity from the vaccine, benefit from vaccination and will be protected from the disease. This is known as herd immunity—where sufficient immunization coverage prevents the transmission of the disease to an otherwise susceptible population. This is especially important for the young, the elderly and those with compromised immune systems.

Because vaccines are given to healthy people, including children, there can be concerns over the possible risks associated with them. While some negative reactions after vaccination can be attributable to the vaccine itself, many are unrelated. Numerous research studies have shown that the risk of not immunizing a community against certain communicable diseases is far greater than the perceived risk of the vaccination. Vaccines are highly studied before they are used in the general population and highly regulated after approval. Biopharmaceutical researchers are focused on continuing to improve the safety and delivery of vaccines for healthy communities.

Today, there are 204 active clinical trials for vaccines, including 107 that have not yet started recruiting patients or are just now seeking volunteers to participate and another 97 that are active, but not recruiting new patients. Those interested in obtaining more information about these vaccine clinical trials, go to ***www.clinicaltrials.gov***, the clinical tests database of the National Institutes of Health.

Scientific Advances in Vaccine Development

Using promising new scientific approaches, researchers are building on the successful history of vaccination against infectious diseases. For example, advances in areas such as genomics are enabling researchers to develop therapeutic vaccines including immunotherapies for some types of cancer and other diseases and conditions. In addition, vaccines today are not limited to injectables—new delivery methods include nasal sprays, powders and transdermal applications, among others. Some recent examples of scientific advances include:

Therapeutic Cancer Vaccines

There are varied approaches to creating a vaccine to treat cancer—they can boost the body's immune response to fight

Recent Successes in Vaccine Use

BROADENING PROTECTION AGAINST SHINGLES

- *Shingles is caused by the same virus (varicella-zoster virus) that causes chickenpox in childhood. In patients that develop shingles, it can lay dormant in certain nerves for years and flare-up in adults causing severe pain and blisters that can last for a very long time. Shingles tends to affect older people and those with weakened immune systems. A vaccine approved in 2006 for people age 60 and older was recently approved to include people 50-59 years of age. About 200,000 people between the ages of 50-59 get shingles each year.*

PROTECTING NEWBORNS FROM PERTUSSIS

- *Pertussis (whooping cough) is a very contagious bacterial disease and one of the most commonly occurring vaccine-preventable diseases in the United States. In recent years, reported pertussis cases have been on the rise—there were more than 40,000 reported cases in 2012—and the Advisory Committee on Immunization Practices (ACIP) now recommends that all pregnant women receive the Tdap vaccine (tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine). Vaccinating women during pregnancy will stimulate maternal anti-pertussis antibodies that should pass to the newborn providing protection against pertussis until they are old enough to be vaccinated themselves. Prior to this recommendation, only pregnant women who never received the Tdap vaccine received the vaccine.*

cancer, they can stop the cancer from growing or slow its growth, and can assist the immune system to locate and kill the cancer. Two immunotherapy vaccines have been recently approved by the Food and Drug Administration, one for the treatment of prostate cancer and the other for melanoma.

Unraveling the Mystery of Deadly Bacteria

Scientists have identified the reason some humans are particularly susceptible to infection by the bacterium *Staphylococcus aureus* or staph—which kills about 100,000 Americans each year. Researchers at Vanderbilt University recently reported that genetic variations in human hemoglobin can make certain people resistant to staph infections.

Vaccine Combinations to Prevent and Treat HIV infection

Recent research provides insight into how immune response provides protection against HIV infection. In a preclinical study, novel vaccine combinations were found to provide partial protection against HIV infection and some combinations substantially reduced the viral load after infection.

New Methods for Vaccine Development

Live recombinant vaccines use an attenuated (weakened) virus from one disease as the delivery vehicle for another infectious disease. This approach is used to enhance the immune response or is used when the virus being treated (such as HIV) is too potent and would actually cause the disease.

DNA vaccines consist of DNA that is coded for a specific antigen—a protein to which the immune system will respond. The DNA vaccine is injected into the body where it produces the antigen and elicits an immune response against the antigen.

New Delivery Methods

Researchers are running preclinical studies looking at using a stomach bacterium to deliver vaccines through food, like yogurt or drinkable liquids. Harmful genes are removed from the bacterium and replaced with those from the virus, such as influenza, to stimulate an immune response in the individual.

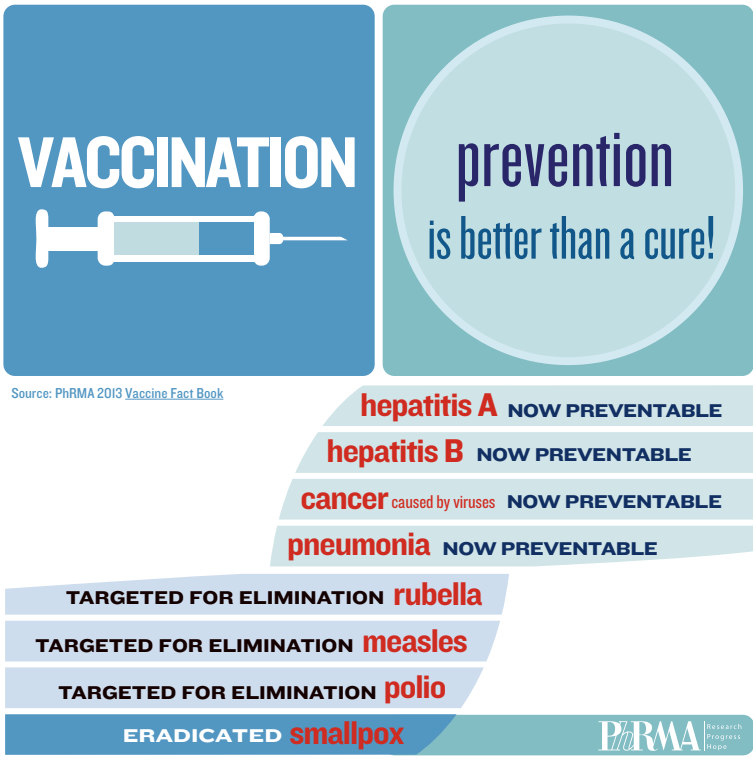
Other new delivery methods include inhalable powders, nasal sprays, a transdermal patch that contains several microscopic needles that delivers the vaccine instead of a syringe; and a vaccine that is not rendered ineffective if stored at warmer temperatures, making it useful in areas where cold storage is limited.

Egg-free Influenza Vaccines

Historically, vaccines against influenza were grown in fertilized chicken eggs, leading to long development times, which make it difficult to respond to public health emergencies such as the "swine flu" pandemic in 2009 and ensure enough supply of the seasonal flu vaccine each year. Egg-free vaccines are also important in that they provide a viable treatment option to those with egg allergies.

In 2012, the first cell-culture-derived vaccine was approved to protect against seasonal influenza in adults. It is manufactured using full-scale cell-culture technology, an alternative to traditional egg-based production. Cell-culture technology uses a mammalian cell line rather than chicken eggs to grow virus strains.

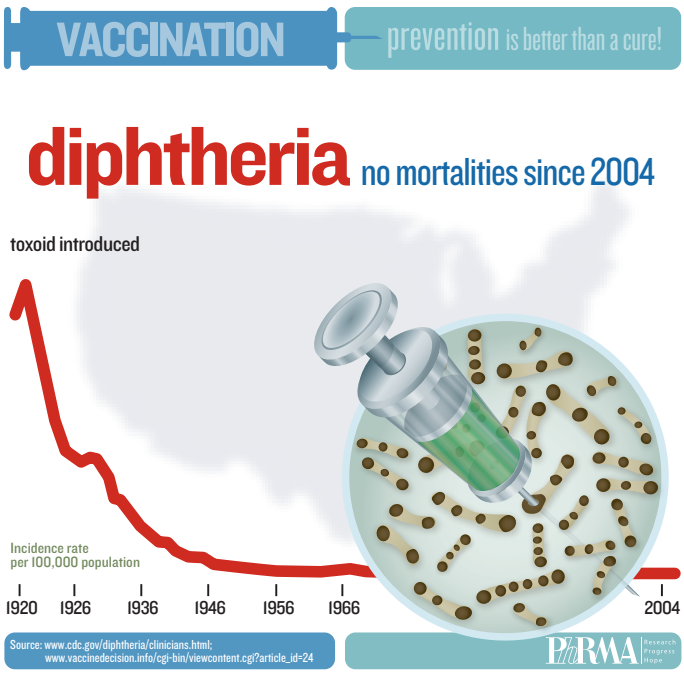
This year the first 100 percent egg-free influenza vaccine was approved for the prevention of influenza in adults. It is a novel protein recombinant vaccine for the prevention of seasonal influenza disease and is the first to be made in a 100 percent egg-free system without growing influenza viruses, so it can be made quickly and without the risk of infections.



Vaccine Successes in the United States

Overview

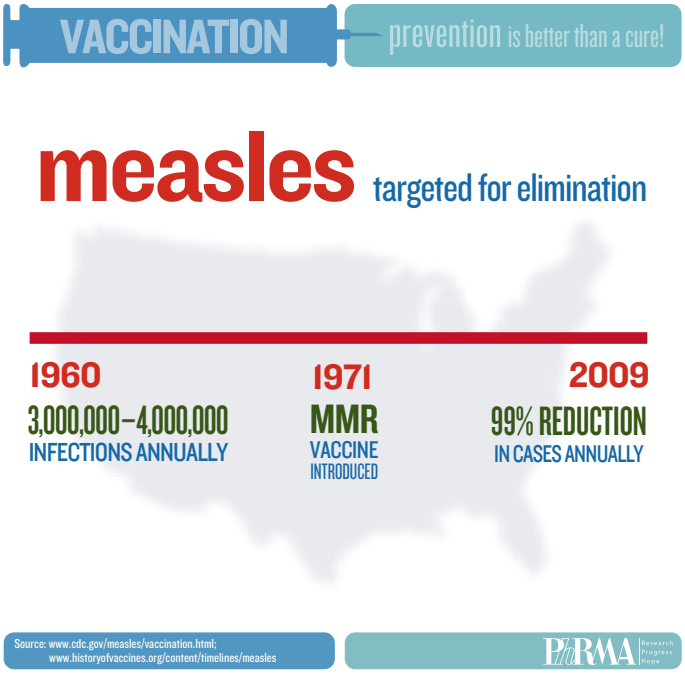
- The current U.S. vaccination schedule for children between birth and age 6 recommends immunizations for 14 different diseases. Each disease for which vaccinations are recommended can cause serious illness or death in unvaccinated populations, and those diseases might quickly begin to appear again if vaccination rates drop. The United States has seen **mumps** outbreaks in recent years since vaccination rates have dropped, with severe complications and hospitalizations required for some patients. And before the introduction of the **Hib (*Haemophilus influenzae* type b) vaccine**, Hib **meningitis** affected more than 12,000 American children annually, killing 600 and leaving many others with seizures, deafness, and developmental disabilities. After introduction of the vaccine, the number of deaths from Hib dropped to fewer than 10 per year.
- Most vaccines prove to be highly effective. After receiving the second dose of the **MMR vaccine (measles, mumps and rubella)** or the stand-alone measles vaccine, 99.7 percent of vaccinated individuals are immune to measles. The inactivated polio vaccine offers 99 percent effectiveness after three doses. The **varicella (chickenpox) vaccine** is between 85 percent and 90 percent effective in preventing all varicella infections, but 100 percent effective in preventing moderate and severe chicken pox.



- **Measles** infection causes encephalitis (inflammation of the brain) for one in 1,000 infected individuals. Overall, measles infection kills two of every 1,000 infected individuals. In contrast, the combination **MMR (measles, mumps and rubella)** vaccine results in a severe allergic reaction only once in every *million* vaccinated individuals, while preventing measles infection. The benefits of vaccine-acquired immunity extraordinarily outweigh the serious risks of infection.
- Before the **varicella vaccine** became available, **chickenpox** infections resulted in 10,000 hospitalizations and caused more than 100 deaths each year in the United States. Even uncomplicated cases of chickenpox cause children to miss a week or more of school, with a caregiver missing work to care for the sick child.

Diseases Covered by Vaccines in the United States

- **Diphtheria** once was a major cause of illness and death among children. The United States recorded 206,000 cases of diphtheria in 1921, resulting in 15,520 deaths (a case-fatality ratio of 7.5 percent). Diphtheria death rates range from about 20 percent for those under age 5 and over the age of 40, and up to 10 percent for those ages 5–40. Since the introduction of effective immunizations, starting in the 1920s, diphtheria rates have dropped dramatically in the United States and other countries that vaccinate widely. Between 2004 and 2008, no cases of diphtheria were recorded in the United States.
- ***Haemophilus influenzae* type b**, commonly known as Hib, is a bacterium that can cause severe infections, particularly in young children, including meningitis, pneumonia and cellulitis (skin infections). The vaccine protects against the diseases caused by Hib, which are numerous and can be severe. Collectively, these Hib-caused infections are referred to generally as "**Hib disease**." Before the Hib vaccine was introduced in 1985, about 20,000 children younger than age 5 developed severe Hib disease in the United States each year, and about 1,000 died. By 2006, the number of reported Hib cases was down to only 29 for the year. Today, the majority of fatalities from Hib disease are reported in developing countries where the Hib vaccine is not widely used, but fatalities still occur in developed nations when vaccination rates drop.

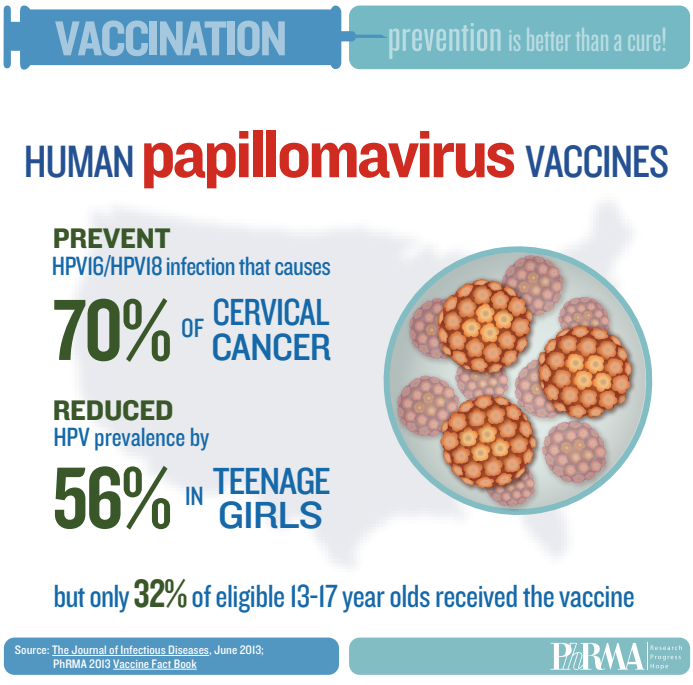


- **Human papillomaviruses (HPV)** belong to a large family of viruses, only some of which are sexually transmitted. Certain types of HPV cause genital warts. Other HPV types are the main cause of cervical cancer, and some are associated with anal, penile, mouth, and throat cancers. HPV is very common: one recent study showed that nearly 27 percent of women ages 14-59 tested positive for one or more strains of HPV. Rates for men are likely to be similar. The U.S. Food and Drug Administration approved a vaccine for four types of HPV in 2006 and another vaccine that protects against two types of HPV in 2009. The recommended age for HPV vaccination of females is 11-12 years. Catch-up vaccination is recommended for females ages 13-26 who have not been previously vaccinated. The vaccine may also be given to males ages 9 through 26 to reduce their likelihood of acquiring genital warts. HPV vaccines have been shown to be most effective when given before exposure to HPV through sexual contact.

- **Measles** is an extremely contagious disease caused by a virus that is easily spread through the air. Its symptoms include fever (which may rise to 104° F or higher) and coughing, as well as its infamous rash. Measles can lead to complications ranging in severity from diarrhea to encephalitis (swelling of the brain), with adult patients typically experiencing more severe complications. Although the disease is rarely fatal in developed countries, the death rate can be quite high in underdeveloped nations. As recently as 2000, measles caused 1.1 million deaths globally among young children in a year. A vaccine to protect against measles was developed in the 1960s and was quickly adopted. Widespread vaccination programs, including the Measles Initiative, launched in 2001 by the American Red Cross, the United Nations Foundation, the U.S. Centers for Disease Control and Prevention, UNICEF and the World Health Organization, contributed to global decreases in measles cases until the case count among children fell as low as 118,000 by 2008. Since 2008, however, vaccination campaigns have suffered from funding cutbacks, allowing the highly contagious disease to roar back, despite the relatively low cost of vaccinating a child against measles (typically less than $1).

- **Mumps** are caused by a virus, and its symptoms include low-grade fever, respiratory problems, and, most notably, swelling of the salivary (parotid) glands below the ear, known as parotitis. While parotitis is the most easily recognized symptom of mumps, it occurs only in about 30 percent to 40 percent of all cases. Up to 20 percent of infected individuals may experience no symptoms at all. In the United States, cases of mumps have dropped by 99 percent since the introduction of a vaccine in 1967. Unlike measles and rubella, however, mumps has not yet been eliminated in the United States.

- **Pertussis**, also known as **whooping cough**, is an extremely contagious disease caused by a bacterium. After symptoms first appear, the disease can take anywhere from



weeks to months to fully run its course. Eventually the patient experiences bouts of rapid coughing followed by the "whooping" sound that gives the disease its common name as they try to inhale. Pertussis can be extremely dangerous for infants and young children, with the highest percentage of complications occurring in children less than 6 months of age. The most common complication is bacterial pneumonia, which is also the most common cause of deaths from pertussis. Although cases of pertussis have dropped dramatically in the United States since the introduction of the pertussis vaccine, the disease has caused widespread outbreaks when vaccination rates have dropped. A recent outbreak in California led to the deaths of five infants in the first six months of 2010.

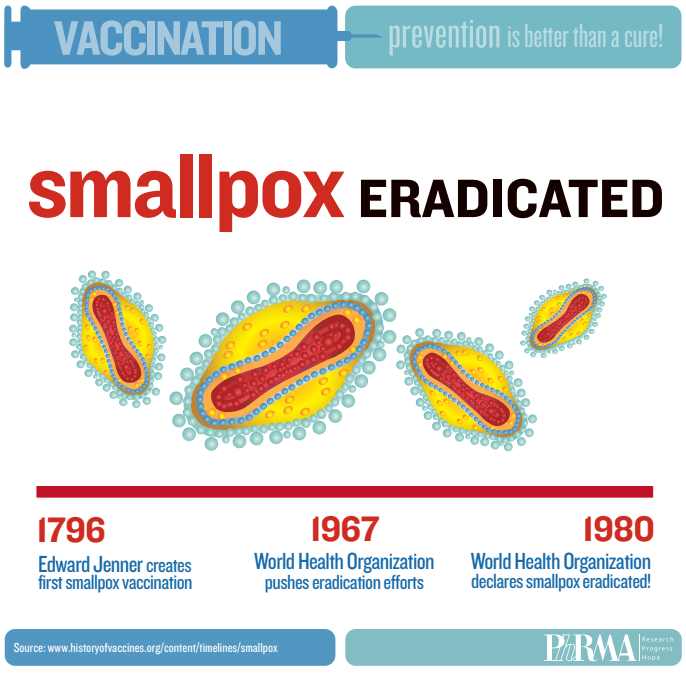
- ***Streptococcus pneumoniae*** bacteria, also called pneumococcal bacteria, are one of the leading causes of illness in young children. At least 90 types of pneumococcal bacteria are known to exist. They can cause pneumonia as well as bloodstream infections (bacteremia), meningitis, sinusitis, and middle ear infection, among other illnesses. Collectively, the different illnesses caused by *Streptococcus pneumoniae* are referred to as **pneumococcal disease**. Invasive pneumococcal disease can be fatal; survivors of meningitis may have permanent injury, including brain damage, seizures, or hearing loss. Each year in the United States, pneumococcal bacteria cause more than 4,800 cases of invasive pneumococcal disease in children younger than age 5. Among this group, about 5 percent die from the infection. Of those who survive, some are left with permanent injury. Pneumococcal bacteremia (bloodstream infection) cases total more than 50,000 each year in the United States (bacteremia occurs in approximately 25 percent of all pneumococcal pneumonia cases). The mortality rate for those with pneumonia complicated by bacteremia is approximately 20 percent, but may be as high as 60 percent for elderly patients. Pneumococcal meningitis cases total about 3,000 each year in the United States, and the mortality rate ranges from 10 percent to 30 percent. A pneumococcal vaccine that protected against 14 different strains was licensed in 1977 and was expanded to protect against 23 strains in 1983. However, it is most effective in adults. A separate vaccine for children was licensed in 2000 and was expanded to include protection against 13 strains in 2010. Since the initial recommendation, invasive pneumococcal disease in children has dropped by nearly 80 percent in the United States.

- Few diseases frightened parents more in the early part of the 20th century than did **polio** (the common name for *poliomyelitis*). Polio tended to strike in the warm summer months, sweeping through a few towns as an epidemic every few years. Though most people recovered quickly from polio, some suffered temporary or permanent paralysis and even death. Many polio survivors were disabled for life. Polio has no cure, so prevention is the most effective means to combat it. In about 95 percent of all polio cases, the person has no symptoms at all. The rest of polio cases can be divided into three types: abortive polio (mild illness), non-paralytic polio (mild illness with neurological symptoms), and paralytic polio (includes the first signs of paralysis). Fewer than 1 percent to 2 percent of people who contract polio become paralyzed. In most cases of paralytic polio, the patient recovers completely. However, for a certain number of people, paralysis or muscle weakness remains for life. In severe cases of paralytic polio, the throat and chest may be paralyzed. Death may result if the patient does not receive artificial breathing support. Between 2 percent to 5 percent of children affected with paralytic polio die; for adults, 15 percent to 30 percent die. Because of widespread vaccination, polio was eliminated from the Western Hemisphere in 1994. Today, it continues to circulate in a handful of countries, with occasional spread to neighboring countries. (Endemic countries are Afghanistan, India, Nigeria, and Pakistan.) Vigorous vaccination programs are being conducted to eliminate these last pockets. Polio vaccination is still recommended worldwide because of the risk of imported cases.

- **Rotavirus** is the most common cause of severe diarrhea in children and infants worldwide. Before a vaccine was introduced in the United States, the disease caused more than 400,000 doctor visits and 200,000 emergency room visits each year, resulting in as many as 60 deaths annually in children younger than age 5. Globally, rotavirus kills more than 500,000 children under age 5 each year, with most deaths occurring in developing countries. In 2006, the newly licensed rotavirus vaccine RotaTeq was recommended as routine infant immunization and in 2008, the Food and Drug Administration licensed another rotavirus vaccine, Rotarix, for use in infants in the United States. The CDC has carefully monitored incidence of rotavirus disease in the United States since 2000. Their studies show that the number of positive test results for rotavirus was substantially lower than the median observed during 2000-2006.

- **Rubella** is caused by a virus, and although rubella is sometimes called "German measles," the rubella virus is not related to the measles virus. Rubella symptoms include low-grade fever, respiratory problems, and most notably a rash of pink or light red spots. In children, illness from rubella infection is usually mild. Complications from rubella are more common in adults. A woman who contracts rubella infection during pregnancy can pass the infection to the developing fetus. Such pregnancies are at risk of spontaneous abortion or premature birth. If the fetus survives, the child may suffer from a wide range of birth defects, including deafness, eye defects, cardiac defects, mental retardation, bone lesions, and other abnormalities. Together, the defects are known as congenital rubella syndrome (CRS), which is the chief danger of rubella disease. From 1964-1965, before the development of a vaccine against the disease, a rubella epidemic swept the United States. During that short period, 12.5 million cases of rubella developed, and 20,000 children were born with CRS: 11,000 were deaf, 3,500 blind, and 1,800 mentally retarded. As of 2004, rubella was declared eliminated in the United States.

- The history of **smallpox**, which is caused by a virus, holds a unique place in human health and medicine. One of the deadliest diseases known to humans, smallpox is also the only disease to have been eradicated by vaccination. Some estimates indicate that worldwide deaths from smallpox numbered more than 300 million during the 20th century. The last U.S. wild smallpox case occurred in 1949. After intensive vaccination campaigns in the 1960s and 1970s, the last case of wild smallpox in the world occurred in Somalia in 1977. (Today, certain U.S. military personnel and some civilian workers receive the smallpox vaccine due to the threat of bioterrorism.)



- **Tetanus** is a disease of the nervous system caused by bacteria. The symptoms of tetanus include lockjaw (the most recognizable of its physical effects), stiffness, and problems swallowing. Later symptoms include severe muscle spasms, seizure-like activity, and severe nervous system disorders. Generally, between 10 percent and 20 percent of tetanus cases result in death, though fatalities are more likely among patients older than age 60 and among unimmunized individuals. The extreme rarity of tetanus cases among individuals immunized up to 10 years prior to infection suggests an efficacy rate of nearly 100 percent for the tetanus vaccine. Immunity levels do decrease with time, however, so that boosters against tetanus are recommended every 10 years in order to maintain protection against the disease.

- **Yellow fever** is a viral disease spread by the bite of infected mosquitoes. Globally, the disease infects about 200,000 people per year, causing fever, chills, nausea, vomiting, muscle pain, and headache, and has no cure. While many yellow fever patients recover after 3-4 days of symptoms, approximately 15 percent enter a second phase of the illness after a remission. The second phase includes a return of high fever, as well as jaundice; abdominal pain and vomiting; bleeding from the mouth, nose, eyes, or stomach; and deteriorating kidney function. Up to half of the patients who experience the second phase may die. In all, yellow fever kills 30,000 people globally each year. The yellow fever vaccine provides protection for 30 years or more—possibly for life—and for 95 percent of those vaccinated, offers protective immunity against the disease within a week. Yellow fever vaccination is typically performed only in areas where the disease is endemic, but it is available (and sometimes required) for those traveling to regions where the virus is still widespread.

Source:

"The History of Vaccines," A Project of the College of Physicians of Philadelphia, *www.historyofvaccines.org*

Allergy

Product Name	Sponsor	Indication	Development Phase*
Cat-SPIRE (cat allergy vaccine)	Circassia *Oxford, United Kingdom*	hypersensitivity to cat dander	Phase III www.circassia.co.uk
CYT003 (toll-like receptor 9 agonist/ Immunodrug™ vaccine)	Cytos Biotechnology *Schlieren, Switzerland*	allergic asthma (monotherapy)	Phase II www.cytos.com
DBV-712 (peanut allergy epicutaneous immunotherapy)	DBV Technologies *Bagneux, France*	peanut hypersensitivity (Fast Track)	Phase II www.dbv-technologies.com
EMP-123 (peanut allergy vaccine)	Allertein Therapeutics *Fairfield, CT*	peanut hypersensitivity	Phase I completed
grass pollen extract sublingual vaccine	Stallergenes *Norwell, MA*	seasonal allergic rhinitis	application submitted www.stallergenes.us
JRC-LAMP vaccine	Immunomics Therapeutics *Hershey, PA*	Japanese red cedar pollen allergy	Phase I www.immunomix.com
MK-3641 (ragweed allergy vaccine sublingual tablet)	Merck *Whitehouse Station, NJ*	seasonal allergic rhinitis	application submitted www.merck.com
MK-7243 (grass pollen allergy immunotherapy tablet vaccine)	Merck *Whitehouse Station, NJ*	seasonal allergic rhinitis --- seasonal allergic rhinitis (pediatric)	application submitted www.merck.com --- Phase III www.merck.com
MK-8237 (house dust mite allergy immunology tablet vaccine)	Merck *Whitehouse Station, NJ*	allergic rhinitis, allergic rhinoconjunctivitis --- allergic asthma	Phase III www.merck.com --- Phase II www.merck.com
Pollinex® Quattro Grass injectable MPL allergy vaccine	Allergy Therapeutics *West Sussex, United Kingdom*	prevention of grass pollen hypersensitivity	Phase III www.allergytherapeutics.com
Pollinex® Quattro Ragweed injectable MPL allergy vaccine	Allergy Therapeutics *West Sussex, United Kingdom*	prevention of ragweed pollen hypersensitivity	Phase III www.allergytherapeutics.com
Pollinex® Quattro Tree injectable MPL allergy vaccine	Allergy Therapeutics *West Sussex, United Kingdom*	prevention of tree pollen hypersensitivity	Phase II www.allergytherapeutics.com
QGE031 (anti-IgE antibody)	Novartis Pharmaceuticals *East Hanover, NJ*	allergic asthma (see also other)	Phase II www.novartis.com

*For more information about a specific medicine or company in the report, please use the website provided.

Allergy

Product Name	Sponsor	Indication	Development Phase
ragweed allergy immunotherapy vaccine	Stallergenes *Norwell, MA*	seasonal allergic rhinitis	Phase I www.stallergenes.us
ragweed allergy vaccine sublingual	Greer Laboratories *Lenoir, NC*	seasonal allergic rhinitis	Phase III www.greerlabs.com

Cancer

Product Name	Sponsor	Indication	Development Phase
abagovomab (mAb therapeutic vaccine) ORPHAN DRUG	Menarini *Florence, Italy*	ovarian cancer	Phase III www.menarini.com
ADXS-HPV (live, attenuated *Listeria* monocytogenes [Lm] vaccine)	Advaxis *Princeton, NJ*	recurrent cervical cancer, cervical intraepithelial neoplasia --- anal cancer	Phase II www.advaxis.com --- Phase I/II www.advaxis.com
AE-O vaccine	Antigen Express *Worcester, MA*	ovarian cancer	Phase I www.antigenexpress.com
AE37 (peptide vaccine)	Antigen Express *Worcester, MA*	breast cancer, prostate cancer	Phase II www.antigenexpress.com
AE-M (peptide vaccine)	Antigen Express *Worcester, MA*	malignant melanoma	Phase I www.antigenexpress.com
AGS-003 (personalized dendritic cell-based vaccine)	Argos Therapeutics *Durham, NC*	first-line kidney cancer (Fast Track) --- metastatic kidney cancer (monotherapy)	Phase III www.argostherapeutics.com --- Phase II www.argostherapeutics.com
AlloStim™ immunotherapeutic vaccine	Immunovative Therapies *Shoham, Israel*	solid tumors	Phase I/II completed www.immunovative.co.il
astuprotimut-R (MAGE-A3 recombinant antigen-specific cancer immunotherapy)	GlaxoSmithKline *Rsch. Triangle Park, NC*	malignant melanoma, non-small-cell lung cancer (NSCLC) --- bladder cancer	Phase III www.gsk.com --- Phase II www.gsk.com

Cancer

Product Name	Sponsor	Indication	Development Phase
AVX701 (CEA-expressing VRP vaccine)	AlphaVax *Rsch. Triangle Park, NC*	advanced or metastatic CEA-expressing colorectal cancer	Phase I/II www.alphavax.com
AVX901 (HER2-expressing VRP vaccine)	AlphaVax *Rsch. Triangle Park, NC*	late-stage HER2-expressing breast cancer	Phase I www.alphavax.com
BiovaxID® dasiprotimut-T (personalized lymphoma vaccine) ORPHAN DRUG	Biovest International *Tampa, FL*	indolent follicular lymphoma (Fast Track) --- mantle-cell lymphoma	Phase III www.biovest.com --- Phase II www.biovest.com
BPX-201 (dendritic cell vaccine)	Bellicum Pharmaceuticals *Houston, TX*	metastatic castration-resistant prostate cancer	Phase I www.bellicum.com
breast cancer vaccine (mAb vaccine)	MabVax Therapeutics *San Diego, CA*	breast cancer	Phase I www.mabvax.com
breast cancer vaccine (HER2/neu therapeutic vaccine)	TapImmune *Seattle, WA*	breast cancer	Phase I www.tapimmune.com
cancer vaccine (autologous idiotype vaccine)	Bayer HealthCare Pharmaceuticals *Wayne, NJ*	follicular lymphoma (prevention of relapse)	Phase I www.bayerpharma.com
cancer vaccine (oral)	Immunitor USA *College Park, MD*	cancer	Phase I/II www.immunitor.com
CB-10-01 (hTRT vaccine)	Cosmo Pharmaceuticals *Lainate, Italy*	malignant melanoma	Phase II www.cosmopharmaceuticals.com
CDX-1401 (mAb cancer vaccine)	Celldex Therapeutics *Needham, MA*	solid tumors expressing the NY-ESO-1 protein	Phase I/II www.celldextherapeutics.com
CG201	CG Therapeutics *Seattle, WA*	solid tumors	Phase II
CRS-207	Aduro BioTech *Berkeley, CA*	metastatic pancreatic cancer (with GVAX pancreas vaccine) --- mesothelioma	Phase II www.adurobiotech.com --- Phase I www.adurobiotech.com
CV-301 breast (immunotherapeutic vaccine)	Bavarian Nordic *Mountain View, CA*	metastatic breast cancer	Phase II www.bavarian-nordic.com
CV-301 colon (immunotherapeutic vaccine)	Bavarian Nordic *Mountain View, CA*	colon cancer	Phase II www.bavarian-nordic.com

Cancer

Product Name	Sponsor	Indication	Development Phase
CV-301 lung (immunotherapeutic vaccine)	Bavarian Nordic *Mountain View, CA*	lung cancer	Phase I www.bavarian-nordic.com
CV-301 ovarian (immunotherapeutic vaccine)	Bavarian Nordic *Mountain View, CA*	ovarian cancer	Phase I www.bavarian-nordic.com
CVac™ MUC-1 cancer vaccine	Prima Biomed *Sydney, Australia*	late stage ovarian cancer	Phase II/III www.primabiomed.com.au
DCVax®-Brain dendritic cell vaccine ORPHAN DRUG	Northwest Biotherapeutics *Bethesda, MD*	glioblastoma	Phase III www.nwbio.com
DCVax®-Head & Neck dendritic cell vaccine	Northwest Biotherapeutics *Bethesda, MD*	head and neck cancer	Phase I completed www.nwbio.com
DCVax®-Liver dendritic cell vaccine	Northwest Biotherapeutics *Bethesda, MD*	liver cancer	Phase I completed www.nwbio.com
DCVax®-Lung dendritic cell vaccine	Northwest Biotherapeutics *Bethesda, MD*	lung cancer	Phase I completed www.nwbio.com
DCVax®-Ovarian dendritic cell vaccine	Northwest Biotherapeutics *Bethesda, MD*	ovarian cancer	Phase I completed www.nwbio.com
DCVax®-Pancreas dendritic cell vaccine	Northwest Biotherapeutics *Bethesda, MD*	pancreatic cancer	Phase I completed www.nwbio.com
DCVax®-Prostate dendritic cell vaccine ORPHAN DRUG	Northwest Biotherapeutics *Bethesda, MD*	prostate cancer	Phase III www.nwbio.com
DN24-02 (lapuleucel-T) (active cellular immunotherapy)	Dendreon *Seattle, WA*	HER2-positive urogenital cancer (adjuvant therapy) --- breast cancer, colorectal cancer, ovarian cancer	Phase II www.dendreon.com --- Phase I www.dendreon.com
DNX-2401 (oncolytic virus vaccine)	DNAtrix *Houston, TX*	glioblastoma	Phase I www.dnatrix.com
DPV-001 (immunotherapy vaccine)	UbiVac *Portland, OR*	NSCLC	Phase II www.ubivac.com
DPX-0907 (single-dose depot vaccine)	Immunovaccine *Halifax, Canada*	breast cancer, ovarian cancer, prostate cancer	Phase II www.imvaccine.com

Cancer

Product Name	Sponsor	Indication	Development Phase
DPX-Survivac (peptide vaccine)	Immunovaccine *Halifax, Canada*	ovarian cancer	Phase I/II www.imvaccine.com
EP-2101 (multi-epitope cancer vaccine)	Biotech Synergy *San Diego, CA*	NSCLC	Phase II
ETBX-011 (adenovirus vector vaccine)	Etubics *Seattle, WA*	colorectal cancer	Phase II www.etubics.com
FANG™ vaccine autologous tumor cell vaccine	Gradalis *Carrollton, TX*	colorectal cancer, malignant melanoma, ovarian cancer	Phase II www.gradalisinc.com
FBP vaccine (folate-binding protein E39 vaccine)	Galena Biopharma *Lake Oswego, OR*	endometrial cancer, ovarian cancer	Phase I/II www.galenabiopharma.com
G-100 prophage cancer vaccine (vitespen) ORPHAN DRUG	Agenus *Lexington, MA*	newly diagnosed glioma	Phase II www.agenusbio.com
G-200 prophage cancer vaccine (vitespen) ORPHAN DRUG	Agenus *Lexington, MA*	recurrent glioma	Phase II www.agenusbio.com
GI-4000 (tarmogen T-cell stimulator)	GlobeImmune *Louisville, CO*	colorectal cancer, NSCLC, pancreatic cancer	Phase II www.globeimmune.com
GI-6207 (tarmogen T-cell stimulator)	GlobeImmune *Louisville, CO*	medullary thyroid cancer	Phase II www.globeimmune.com
GI-6301 (brachyury peptide vaccine)	GlobeImmune *Louisville, CO*	chordoma, metastatic tumors	Phase I www.globeimmune.com
GL-0817 (MAGE-A3 immunomodulator vaccine) ORPHAN DRUG	Gliknik *Baltimore, MD*	head and neck cancer, myeloma	Phase II www.gliknik.com
GRNVAC 1 (dendritic cell vaccine)	Geron *Menlo Park, CA*	acute myeloid leukemia (AML)	Phase II www.geron.com
GV1001 (hTERT RNA vaccine)	KAEL-GemVax *Seoul, South Korea*	pancreatic cancer	Phase I www.kaelgemvax.com
HS-110	Heat Biologics *Chapel Hill, NC*	NSCLC	Phase II www.heatbio.com

Cancer

Product Name	Sponsor	Indication	Development Phase
HyperAcute® Lung tergenpumatucel-L	NewLink Genetics *Ames, IA*	NSCLC	Phase II/III www.linkp.com
HyperAcute® Melanoma lung cancer immunotherapy	NewLink Genetics *Ames, IA*	malignant melanoma	Phase II completed www.linkp.com
HyperAcute® Pancreas algenpantucel-L ORPHAN DRUG	NewLink Genetics *Ames, IA*	pancreatic cancer (Fast Track)	Phase III www.linkp.com
ICT-107 (autologous dendritic cell-based vaccine) ORPHAN DRUG	ImmunoCellular Therapeutics *Woodland Hills, CA*	glioblastoma	Phase II www.imuc.com
ICT-121 (dendritic cell vaccine)	ImmunoCellular Therapeutics *Woodland Hills, CA*	glioblastoma	Phase I www.imuc.com
IMA901 (multi tumor-associated peptides cancer vaccine) ORPHAN DRUG	immatics biotechnologies *Tuebingen, Germany*	kidney cancer	Phase III www.immatics.com
IMA950 (tumor-associated peptide vaccine)	immatics biotechnologies *Tuebingen, Germany*	glioblastoma	Phase I www.immatics.com
IMCgp100	Immunocore *Oxon, United Kingdom*	malignant melanoma	Phase 0 www.immunocore.com
IMF-001 (protein vaccine)	ImmunoFrontier *Tokyo, Japan*	solid tumors	Phase I www.immunofrontier.com
IMT-1012 (multi-peptide antigen immunotherapeutic vaccine)	Immunotope *Doylestown, PA*	breast cancer, ovarian cancer	Phase I www.immunotope.com
ISF35 (recombinant immunotherapy)	Memgen *San Diego, CA*	chronic lymphocytic leukemia (CLL) (monotherapy), non-Hodgkin's lymphoma --- CLL (combination therapy)	Phase II www.memgenbio.com --- Phase I www.memgenbio.com
M-200 prophage cancer vaccine (vitespen) ORPHAN DRUG	Agenus *Lexington, MA*	malignant melanoma	Phase III www.agenusbio.com

Cancer

Product Name	Sponsor	Indication	Development Phase
melanoma mAb vaccine	MabVax Therapeutics *San Diego, CA*	melanoma	Phase I www.mabvax.com
melapuldencel-T (cancer immunotherapy vaccine)	California Stem Cell *Irvine, CA*	malignant melanoma	Phase II www.californiastemcell.com
MVA-BN® HER2 HER-2/neu-based modified vaccinia ankara (MVA) vaccine	Bavarian Nordic *Mountain View, CA*	breast cancer	Phase I/II www.bavarian-nordic.com
MVA-BN® PRO PSA/PAP-based modified vaccinia anakara (MVA) vaccine	Bavarian Nordic *Mountain View, CA*	prostate cancer	Phase I/II www.bavarian-nordic.com
neuroblastoma vaccine	MabVax *San Diego, CA*	neuroblastoma	Phase I www.mabvax.com
NeuVax™ E75 cancer vaccine (nelipepimut)	Galena Biopharma *Lake Oswego, OR*	node-positive breast cancer --- node-negative breast cancer --- prostate cancer	Phase III www.galenabiopharma.com --- Phase II www.galenabiopharma.com --- Phase II www.galenabiopharma.com
Oncophage® vitespen ORPHAN DRUG	Agenus *Lexington, MA*	renal cell carcinoma (Fast Track)	Phase III www.agenusbio.com
OncoVAX® colorectal cancer vaccine	Vaccinogen *Frederick, MD*	stage II colorectal cancer --- stage III colorectal cancer (Fast Track) --- kidney cancer, melanoma	Phase III completed www.vaccinogeninc.com --- Phase II www.vaccinogeninc.com --- Phase I/II www.vaccinogeninc.com
ONT-10 (therapeutic vaccine)	Oncothyreon *Seattle, WA*	solid tumors	Phase I www.oncothyreon.com
OPT-822 (immunotherapy vaccine)	Optimer Pharmaceuticals *San Diego, CA*	breast cancer	Phase II/III www.optimerpharma.com
oregovomab ORPHAN DRUG	Quest PharmaTech *Edmonton, Canada*	ovarian cancer	Phase II www.questpharmatech.com
ovarian cancer mAb vaccine	MabVax Therapeutics *San Diego, CA*	ovarian cancer	Phase II www.mabvax.com

Cancer

Product Name	Sponsor	Indication	Development Phase
ovarian cancer stem cell therapy	California Stem Cell *Irvine, CA*	ovarian cancer	Phase I www.californiastemcell.com
PEK fusion protein vaccine	HealthBanks Biotech USA *Irvine, CA*	cervical intraepithelial neoplasia	Phase I www.healthbanks.com.tw
POL-103A (polyvalent shed-antigen vaccine) ORPHAN DRUG	Polynoma *San Diego, CA*	malignant melanoma	Phase III www.polynoma.com
polyclonal antibody stimulator ORPHAN DRUG	Cancer Advances *Durham, NC*	gastric cancer, pancreatic cancer --- colorectal cancer	Phase III www.canceradvancesinc.com --- Phase II www.canceradvancesinc.com
PRAME antigen-specific cancer immunotherapeutic	GlaxoSmithKline *Rsch. Triangle Park, NC*	malignant melanoma, NSCLC	Phase I www.gsk.com
Prostvac® rilimogene galvacivepvac	Bavarian Nordic *Mountain View, CA*	metastatic prostate cancer (Fast Track)	Phase III www.bavarian-nordic.com
Provenge® sipuleucel-T	Dendreon *Seattle, WA*	recurrent early-stage prostate cancer --- early-stage prostate cancer (neoadjuvant therapy)	Phase III www.dendreon.com --- Phase II www.dendreon.com
PSMA vaccine	AlphaVax *Rsch. Triangle Park, NC*	prostate cancer	Phase I www.alphavax.com
PT107 (allogeneic tumor cell vaccine)	Pique Therapeutics *Durham, NC*	NSCLC	Phase II www.piquetherapeutics.com
PVX-410 (therapeutic cancer vaccine)	OncoPep *North Andover, MA*	smoldering myeloma	Phase I/II www.oncopep.com
REIC gene therapy (reduced expression in immortalized cells)	Momtaro-Gene *Okayama, Japan*	prostate cancer	Phase I www.mt-gene.com
rindopepimut (EGFR varient III vaccine) ORPHAN DRUG	Celldex Therapeutics *Needham, MA*	first-line glioblastoma (Fast Track) --- recurrent glioblastoma (Fast Track)	Phase III www.celldextherapeutics.com --- Phase II www.celldextherapeutics.com

Cancer

Product Name	Sponsor	Indication	Development Phase
sarcoma mAb vaccine	MabVax Therapeutics *San Diego, CA*	sarcoma	Phase II www.mabvax.com
SL-701 (dendritic cell vaccine)	Stemline Therapeutics *New York, NY*	glioma	Phase I/II www.stemline.com
small-cell lung cancer mAb vaccine	MabVax Therapeutics *San Diego, CA*	small-cell lung cancer (SCLC)	Phase I www.mabvax.com
tecemotide (L-BLP25) (MUC1 antigen-specific cancer immunotherapy)	EMD Serono *Rockland, MA* Oncothyreon *Seattle, WA*	NSCLC (Fast Track)	Phase III www.emdserono.com www.oncothyreon.com
TeloB-Vax telomerase cancer vaccine	Adamis Pharmaceuticals *San Diego, CA*	prostate cancer	Phase I www.adamispharma.com
TVI-Brain-1 (cellular immunotherapy vaccine)	TVAX Biomedical *Lenexa, KS*	glioma	Phase II www.tvaxbiomedical.com
TVI-Kidney-1 (cellular immunotherapy vaccine)	TVAX Biomedical *Lenexa, KS*	renal cell carcinoma	Phase II www.tvaxbiomedical.com
V503 (virus-like particle [VLP] vaccine)	Merck *Whitehouse Station, NJ*	HPV-related cancers (see also infectious diseases)	Phase III www.merck.com
V930/V932 (cancer vaccine)	Merck *Whitehouse Station, NJ*	cancer	Phase I completed www.merck.com
V935 (telomerase inhibitor vaccine)	Geron *Menlo Park, CA* Merck *Whitehouse Station, NJ*	solid tumors	Phase I www.geron.com www.merck.com
VGX-3100 (HPV type 16/18 DNA vaccine)	Inovio Pharmaceuticals *Blue Bell, PA*	cervical dysplasia (see also infectious diseases)	Phase II www.inovio.com
WT1 antigen-specific cancer immunotherapeutic	GlaxoSmithKline *Rsch. Triangle Park, NC*	breast cancer	Phase I/II www.gsk.com
WT2527 (peptide vaccine)	Sunovion Pharmaceuticals *Marlborough, MA*	hematological malignancies, solid tumors	Phase I www.sunovion.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
ACAM529	Sanofi Pasteur *Swiftwater, PA* National Institute of Allergy and Infectious Diseases *Bethesda, MD*	herpes simplex virus (HSV) infection	Phase I www.sanofi.com
ACAM-Cdiff (toxoid vaccine)	Sanofi Pasteur *Swiftwater, PA*	prevention of *Clostridium difficile* infection (Fast Track)	Phase III www.sanofi.com
ACE527 (ETEC vaccine)	TD Vaccines *Odense, Denmark* PATH *Seattle, WA*	prevention of traveler's diarrhea caused by *Escherichia coli* infection	Phase II www.tdvaccines.com www.path.org
acellular pertussis vaccine	Novartis Vaccines *Cambridge, MA*	prevention of diphtheria, tetanus and pertussis	Phase I completed www.novartisvaccines.com
ADVAX (DNA vaccine)	Aaron Diamond AIDS Research Center *New York, NY* International AIDS Vaccine Initiative *New York, NY* Ichor Medical Systems *San Diego, CA*	HIV infection prevention --- HIV infection prevention (new delivery system)	Phase I completed www.adarc.org www.iavi.org www.ichorms.com --- Phase I completed www.adarc.org www.iavi.org www.ichorms.com
AE-AI vaccine	Antigen Express *Worcester, MA*	prevention of avian flu	Phase I www.antigenexpress.com
AE-H vaccine	Antigen Express *Worcester, MA*	prevention and treatment of HIV infection	Phase I www.antigenexpress.com
Aflunov™ influenza A virus H5N1 vaccine (flu cell culture)	Novartis Vaccines *Cambridge, MA*	prevention of influenza A virus H5N1 subtype (pre-pandemic)	Phase II www.novartisvaccines.com
AGS-004 (personalized dendritic cell-based vaccine)	Argos Therapeutics *Durham, NC*	HIV-1 infection	Phase II www.argostherapeutics.com
anthrax vaccine (oral)	National Institute of Allergy and Infectious Diseases (NIAID) *Bethesda, MD* PaxVax *San Diego, CA*	prevention of anthrax	Phase I www.paxvax.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
ASP-0113 (plasma DNA-based vaccine) ORPHAN DRUG	Astellas Pharma US *Northbrook, IL* Vical *San Diego, CA*	prevention of cytomegalovirus (CMV) infection	Phase III www.astellas.com www.vical.com
AVX101 (monovalent HIV vaccine)	AlphaVax *Rsch. Triangle Park, NC*	prevention of HIV-1 infection	Phase I completed www.alphavax.com
AVX502 (influenza vaccine)	AlphaVax *Rsch. Triangle Park, NC*	influenza (young adults and elderly)	Phase I www.alphavax.com
AVX601 (cytomegalovirus vaccine)	AlphaVax *Rsch. Triangle Park, NC* Novartis Vaccines *Cambridge, MA*	prevention of CMV infection	Phase I www.alphavax.com www.novartisvaccines.com
Bexsero® meningococcal vaccine group B quadrivalent recombinant vaccine	Novartis Vaccines *Cambridge, MA*	meningococcal group B infection	Phase II www.novartisvaccines.com
BioThrax® anthrax vaccine adsorbed (subcutaneous)	Emergent BioSolutions *Rockville, MD*	anthrax (post-exposure prevention) (Fast Track)	Phase III www.emergentbiosolutions.com
CR6261 (mAb/influenza vaccine)	CruCell *Leiden, Netherlands*	treatment of influenza A virus infection	Phase I www.crucell.com
DCVax-001/CD-2401 (recombinant protein vaccine)	Celldex Therapeutics *Needham, MA* Rockefeller University *New York, NY*	prevention and treatment of HIV infection	Phase I www.celldextherapeutics.com
dengue DNA vaccine	U.S. Naval Medical Research Center *Silver Spring, MD* Vical *San Diego, CA*	prevention of dengue fever	Phase I www.vical.com
dengue fever vaccine	Sanofi Pasteur *Swiftwater, PA*	prevention of mild to severe dengue fever (Fast Track)	Phase III www.sanofi.com
dengue vaccine (TDENV-PIV)	GlaxoSmithKline *Silver Spring, MD* U.S. Army Medical Research and Materiel Command *Fort Detrick, MD*	prevention of dengue fever	Phase I www.gsk.com
DENVax™ tetravalent hybrid dengue virus vaccine	Inviragen *Fort Collins, CO*	dengue	Phase II www.inviragen.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
DermaVir™ Patch DNA topical patch vaccine	Genetic Immunity *McLean, VA*	treatment of HIV-1 infection	Phase II www.geneticimmunity.com
DTP-HepB-Polio-Hib hexavalent vaccine (PR5IV419)	Merck *Whitehouse Station, NJ* Sanofi Pasteur *Swiftwater, PA*	diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis, *Haemophilus influenzae* type b (pediatric)	Phase III www.merck.com www.sanofi.com
Ebola DNA vaccine	Crucell *Leiden, Netherlands* Vaccine Research Center (NIAID) *Bethesda, MD*	prevention of Ebola virus infection	Phase I www.crucell.com
Fluad® influenza virus vaccine (H1N1/H3N2/type-B strains)	Novartis Vaccines *Cambridge, MA*	influenza virus infection (children and elderly)	Phase III www.novartisvaccines.com
Fluzone® QIV ID quadrivalent inactivated influenza vaccine intradermal	Sanofi Pasteur *Swiftwater, PA*	influenza virus infection	Phase III www.sanofi.com
FVH1 DNA-based influenza vaccine	Inovio Pharmaceuticals *Blue Bell, PA*	influenza A virus H1N1 subtype	Phase I www.inovio.com
GelVac™ H5N1 influenza virus vaccine-nasal dry powder	Nanotherapeutics *Alachua, FL*	influenza virus infection	Phase I www.nanotherapeutics.com
GEN-003 (herpes simplex virus type-2 therapeutic vaccine)	Genocea Biosciences *Cambridge, MA*	treatment of HSV infection	Phase I/II www.genocea.com
GI-5005 (tarmogen T-cell immunity stimulator)	GlobeImmune *Louisville, CO*	hepatitis C virus (HCV) infection	Phase II www.globeimmune.com
GS-4774/GI-13020 (tarmogen T-cell immunity stimulator)	Gilead *Foster City, CA* GlobeImmune *Louisville, CO*	chronic hepatitis B virus (HBV) infection	Phase I www.gilead.com www.globeimmune.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
GSK134612 (MenACWY-TT conjugated vaccine)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of meningococcal groups A, C, Y and W-135 infections (children) --- prevention of meningococcal groups A, C, Y and W-135 infections (adults, adolescents, infants)	Phase III www.gsk.com --- Phase II www.gsk.com
GSK2392102A (*Staphylococcus aureus* vaccine)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of staphylococcal infection	Phase I www.gsk.com
GSK2654909A (immunostimulant vaccine)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of H9N2 avian influenza virus infection	Phase I www.gsk.com
GSK2654911A (immunostimulant vaccine)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of H9N2 avian influenza virus infection	Phase I www.gsk.com
GSK3003891A (immunostimulant vaccine)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of respiratory syncytial virus (RSV) infection	Phase I www.gsk.com
H1N1 seasonal influenza virus vaccine	Vaxart *San Francisco, CA*	prevention of seasonal H1N1 influenza virus infection	Phase I www.vaxart.com
H5N1 (pre-)pandemic influenza virus vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of influenza A virus H5N1 subtype (pandemic use in adults) --- prevention of influenza A virus H5N1 subtype (pediatric pandemic use)	application submitted www.gsk.com --- Phase III www.gsk.com
H5N1 influenza vaccine (recombinant VLP vaccine)	Novavax *Rockville, MD*	prevention of influenza A virus H5N1 subtype (seasonal use) --- prevention of influenza A virus H5N1 subtype (pandemic use)	Phase II www.novavax.com --- Phase I www.novavax.com
H5N1 influenza virus vaccine	Vaxart *San Francisco, CA*	prevention of influenza A virus H5N1 subtype	Phase I www.vaxart.com
HBV-002 (recombinant subunit vaccine)	Hawaii Biotech *Aiea, HI*	prevention of West Nile virus infection	Phase I completed www.hibiotech.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
hepatitis C vaccine therapy (Ad6NSmut)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of HCV	Phase I/II www.gsk.com
Heplisav™ hepatitis B vaccine 1018-ISS conjugate	Dynavax *Berkeley, CA*	prevention of HBV	application submitted www.dynavax.com
HerpV herpes simplex vaccine	Agenus *Lexington, MA*	treatment of HSV-2 infection	Phase II www.agenusbio.com
HibTITER™ Hib CRM197 conjugate vaccine	Nuron Biotech *Exton, PA*	prevention of *Haemophilus influenzae* type B infection (pediatric)	Phase II www.nuronbiotech.com
HIV recombinant vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	HIV disease immunotherapy	Phase II www.gsk.com
HIV recombinant vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of HIV infection	Phase I www.gsk.com
HIV vaccine	Crucell *Leiden, Netherlands* Beth Israel Deaconess Medical Center *Boston, MA* International AIDS Vaccine Initiative *New York, NY*	prevention of HIV infection	Phase I www.crucell.com
HIV vaccine	GeoVax Labs *Smyrna, GA*	prevention of HIV infection	Phase II www.geovax.com
HIV vaccine	GeoVax Labs *Smyrna, GA*	treatment of HIV infection	Phase I/II www.geovax.com
HIV vaccine	PaxVax *San Diego, CA*	prevention of HIV infection	Phase I www.paxvax.com
HIV vaccine	Novartis Vaccines *Cambridge, MA*	HIV infection	Phase I www.novartisvaccines.com
HIV vaccine (MAG pDNA)	Profectus Biosciences *Baltimore, MD*	prevention of HIV infection	Phase I www.profectusbiosciences.com
HIV vaccine (rVSV)	Profectus Biosciences *Baltimore, MD*	prevention of HIV infection	Phase I www.profectusbiosciences.com
HIVAX™ replication-defective HIV-1 vaccine	GeneCure Biotechnologies *Norcross, GA*	HIV-1 infection	Phase I www.genecure.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
IC31 (seasonal influenza vaccine)	Novartis Vaccines *Cambridge, MA* Valneva *Vienna, Austria*	prevention of influenza virus infection	Phase I www.novartisvaccines.com
IC43 (*Pseudomonas aeruginosa* vaccine)	Novartis Vaccines *Cambridge, MA* Valneva *Vienna, Austria*	prevention of nosocomial (hospital-acquired) infection involving *Pseudomonas aeruginosa*	Phase I www.novartisvaccines.com
IC84 (recombinant fusion protein vaccine)	Novartis Vaccines *Cambridge, MA* Valneva *Vienna, Austria*	prevention of *Clostridium difficile* infection	Phase I www.novartisvaccines.com
Imvamune® smallpox vaccine	Bavarian Nordic *Mountain View, CA*	smallpox (liquid formulation) --- smallpox (freeze-dried formulation)	Phase III www.bavarian-nordic.com --- Phase II www.bavarian-nordic.com
influenza A virus H1N1 vaccine (L.E.A.P.S.™)	CEL-SCI *Vienna, VA*	prevention and treatment of influenza A virus H1N1 subtype	Phase I www.cel-sci.com
influenza A virus H3N2 vaccine	Novartis Vaccines *Cambridge, MA*	prevention of influenza A virus H3N2 subtype	Phase I www.novartisvaccines.com
influenza A virus H5N1 cell culture-based vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of influenza A virus H5N1 subtype (pandemic use)	Phase I www.gsk.com
influenza A virus H5N1 vaccine	Baxter Healthcare *Deerfield, IL*	prevention of influenza A virus H5N1 subtype	Phase I www.baxter.com
influenza A virus vaccine H1N1	Medicago USA *Durham, NC*	prevention of influenza A virus H1N1 subtype	Phase I www.medicago.com
influenza A virus vaccine H5N1	Medicago USA *Durham, NC*	prevention of influenza A virus H5N1 subtype	Phase I www.medicago.com
influenza A virus vaccine H5N1	iBio *Newark, DE*	prevention of influenza A virus H5N1 subtype	Phase I www.ibioinc.com
influenza A virus H7N9 vaccine	Novavax *Rockville, MD*	prevention of influenza A virus H7N9 subtype	Phase I www.novavax.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
influenza A virus vaccine H9N2	Baxter Healthcare *Deerfield, IL*	prevention of influenza A virus H9N2 subtype	Phase I/II completed www.baxter.com
INO-3401 (DNA vaccine)	Inovio Pharmaceuticals *Blue Bell, PA*	influenza A virus H5N1 subtype	Phase I completed www.inovio.com
INO-3510 (DNA vaccine)	Inovio Pharmaceuticals *Blue Bell, PA*	influenza A virus H1N1 subtype, influenza A virus H5N1 subtype	Phase I www.inovio.com
INV21 (enterovirus A vaccine)	Inviragen *Fort Collins, CO*	hand, foot and mouth disease	Phase I www.inviragen.com
ITV-1 (immune therapeutic vaccine-1)	Immunotech Laboratories *Monrovia, CA*	HIV infection	Phase I www.immunotechlab.com
LIQ-001	Liquidia Technologies *Rsch. Triangle Park, NC*	influenza virus infection	Phase I completed www.liquidia.com
Lyme disease vaccine	Baxter Healthcare *Deerfield, IL*	prevention of Lyme disease	Phase I/II www.baxter.com
malaria vaccine (recombinant, Ad35-CS)	CruceII *Leiden, Netherlands*	malaria	Phase I completed www.crucell.com
malaria vaccine	GenVec *Gaithersburg, MD* U.S. Naval Medical Research Center *Silver Spring, MD*	malaria	Phase I/II www.genvec.com
malaria vaccine (PfSPZ)	Sanaria *Rockville, MD*	malaria	Phase I/II www.sanaria.com
MEDI-550 (pandemic influenza virus vaccine)	MedImmune *Gaithersburg, MD*	prevention of pandemic influenza	Phase I www.medimmune.com
MEDI-559 (PRVV)	MedImmune *Gaithersburg, MD*	prevention of RSV infection (pediatric)	Phase I www.medimmune.com
MenABCWY multivalent conjugate vaccine	Novartis Vaccines *Cambridge, MA*	prevention of meningococcal groups A, B, C, Y and W-135 infections (adolescents)	Phase II www.novartisvaccines.com
Meninge ACYW second-generation meningococcal conjugate infant vaccine	Sanofi Pasteur *Swiftwater, PA*	meningococcal infection	Phase II www.sanofi.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
MMR vaccine (live attenuated trivalent vaccine) (GSK209762)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of measles, mumps and rubella	Phase III www.gsk.com
Mosquirix™ malaria vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of malaria (*Plasmodium falciparum*)	Phase III www.gsk.com
NB-1008 (intranasal vaccine)	NanoBio *Ann Arbor, MI*	prevention of influenza virus infection	Phase I www.nanobio.com
NDV-3 (recombinant protein vaccine)	NovaDigm Therapeutics *Grand Forks, ND*	prevention of candidiasis, prevention of staphylococcal (MRSA) infection	Phase I www.novadigm.net
NmVac4 (meningococcal vaccine groups ACWY conjugate vaccine)	JN-International Medical *Omaha, NE*	prevention of meningococcal groups A, C, Y, and W-135 infections	Phase I www.jn-vaccines.org
norovirus bivalent vaccine	LigoCyte Pharmaceuticals (Takeda) *Bozeman, MT*	norovirus gastroenteritis	Phase I/II www.takeda.com
NTHi recombinant vaccine (GSK2838497A)	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of non-typeable *Haemophilus influenzae*	Phase I www.gsk.com
NuThrax™ anthrax vaccine adsorbed with CPG 7909 adjuvant	Emergent BioSolutions *Rockville, MD*	anthrax (post-exposure prevention)	Phase II www.emergentbiosolutions.com
Optaflu® influenza virus vaccine (flu cell culture)	Novartis Vaccines *Cambridge, MA*	prevention of influenza virus infection	Phase III www.novartisvaccines.com
PanBlok® influenza A virus H5N1 vaccine	Protein Sciences *Meridian, CT*	prevention of influenza A virus H5N1 subtype (pandemic)	Phase I/II www.proteinsciences.com
PENNVAX™-B DNA vaccine (clade B)	Inovio Pharmaceuticals *Blue Bell, PA*	prevention and treatment of HIV infection	Phase I www.inovio.com
PENNVAX™-G DNA vaccine (clade A, C, D)	Inovio Pharmaceuticals *Blue Bell, PA*	prevention and treatment of HIV infection	Phase I www.inovio.com
PER.C-flu	Crucell *Leiden, Netherlands*	prevention of influenza virus infection	Phase II www.crucell.com
PF-05212366 (MnB rLP2086)	Pfizer *New York, NY*	meningitis B (adolescent and young adult)	Phase III www.pfizer.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
PF-06290510 (4-antigen *Staphylococcus aureus* vaccine, SA4Ag)	Pfizer *New York, NY*	staphylococcal infection	Phase II www.pfizer.com
PF-06425090	Pfizer *New York, NY*	*Clostridium difficile* colitis	Phase I www.pfizer.com
plague vaccine injectable	DynPort Vaccine *Frederick, MD*	*Yersinia* infection	Phase II completed www.csc.com/dvc
Preflucel™ seasonal influenza virus vaccine	Baxter Healthcare *Deerfield, IL*	prevention of influenza virus infection	Phase III www.baxter.com
PreviThrax® recombinant protective antigen (rPA) anthrax vaccine, purified	Emergent BioSolutions *Rockville, MD*	anthrax (Fast Track)	Phase II www.emergentbiosolutions.com
Pseudomonas aeruginosa antibody fragment product	Sanofi Pasteur *Swiftwater, PA*	prevention of ventilator-associated pneumonia	Phase I www.sanofi.com
PXVX-0103 (influenza A virus vaccine H5N1)	PaxVax *San Diego, CA*	prevention of influenza A virus H5N1 subtype	Phase I www.paxvax.com
PXVX-0200 (oral, live attenuated vaccine)	PaxVax *San Diego, CA*	cholera	Phase I www.paxvax.com
Quadracel® diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed combined with inactivated poliomyelitis vaccine	Sanofi Pasteur *Swiftwater, NJ*	diphtheria, tetanus, pertussis and polio vaccine (in children 4-6 years of age)	Phase III www.sanofi.com
rabies VRVg (purified vero rabies vaccine)	Sanofi Pasteur *Swiftwater, PA*	prevention of rabies infection	Phase II www.sanofi.com
recombinant botulinum neurotoxin vaccine	DynPort Vaccine Company *Frederick, MD* U.S. Department of Defense *Washington, DC*	prevention against botulinum neurotoxin types A and B	Phase II www.csc.com/dvc
respiratory syncytial virus recombinant nanoparticle vaccine	Novavax *Rockville, MD*	prevention of RSV infection	Phase II www.novavax.com

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
rotavirus vaccine (live attenuated tetravalent oral vaccine)	Sanofi Pasteur *Swiftwater, PA*	prevention of rotavirus infection	Phase II www.sanofi.com
SAV001 (genetically attenuated, irradiated and chemically inactivated HIV vaccine)	Sumagen *Seoul, South Korea*	HIV-1 infection	Phase I www.sumagen.co.kr
S. pneumoniae pediatric next-generation recombinant conjugated vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of *Staphylococcus pneumoniae*	Phase II www.gsk.com
S. pneumoniae vaccine	Novartis Vaccines *Cambridge, MA*	pneumococcal infection	Phase I www.novartisvaccines.com
SparVax™ recombinant protective antigen (rPA) anthrax vaccine	PharmAthene *Annapolis, MD*	anthrax (pre- and post-exposure prevention)	Phase II www.pharmathene.com
streptococcal B vaccine conjugate	Novartis Vaccines *Cambridge, MA*	group B streptococcal infection	Phase II www.novartisvaccines.com
Streptococcus pneumoniae vaccine	Sanofi Pasteur *Swiftwater, PA*	meningitis and pneumonia	Phase I www.sanofi.com
TG-4040 (vector-based therapeutic vaccine)	Transgene *Rockville, MD*	hepatitis C	Phase II www.transgene.fr
tuberculosis recombinant subunit vaccine	Sanofi Pasteur *Swiftwater, PA*	prevention of tuberculosis	Phase I www.sanofi.com
tuberculosis recombinant vaccine (GSK692342)	Aeras *Rockville, MD* GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of tuberculosis	Phase II www.aeras.org www.gsk.com
tuberculosis vaccine	Aeras *Rockville, MD* Crucell *Leiden, Netherlands*	prevention of tuberculosis	Phase I www.aeras.org www.crucell.com
tuberculosis vaccine (ID 93/GLA-SE)	Aeras *Rockville, MD* Infectious Disease Research Institute *Seattle, WA*	tuberculosis	Phase I www.aeras.org

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
tularemia vaccine	DynPort Vaccine *Frederick, MD*	prevention of tularemia	Phase I www.csc.com/dvc
typhoid vaccine	Novartis Vaccines *Cambridge, MA*	prevention of typhoid	Phase II www.novartisvaccines.com
V114 (pneumococcal 15-valent conjugate vaccine)	Merck *Whitehouse Station, NJ*	prevention of pneumococcal infection	Phase II www.merck.com
V212 (heat-treated varicella-zoster virus [VZV] vaccine)	Merck *Whitehouse Station, NJ*	prevention of herpes zoster	Phase III www.merck.com
V503 (virus-like particle [VLP] vaccine)	Merck *Whitehouse Station, NJ*	prevention and treatment of HPV infection (see also cancer)	Phase III www.merck.com
Vacc-4x (intradermal vaccine)	Bionor Pharma *Oslo, Norway*	HIV-1 infection	Phase II www.bionorpharma.com
varicella zoster recombinant vaccine	GlaxoSmithKline *Rsch. Triangle Park, NC*	prevention of herpes zoster	Phase III www.gsk.com
VAX-102 (Flagellin.HuHA)	VaxInnate *Cranbury, NJ*	seasonal influenza A virus infection	Phase I/II www.vaxinnate.com
VAX-125 (Flagellin.HuHA)	VaxInnate *Cranbury, NJ*	pandemic influenza A virus infection	Phase II completed www.vaxinnate.com
VAX-128 (recombinant vaccine)	VaxInnate *Cranbury, NJ*	prevention of influenza A virus H1N1 subtype (pandemic)	Phase I www.vaxinnate.com
VAX-161 (recombinant vaccine)	VaxInnate *Cranbury, NJ*	prevention of influenza A virus H5N1 subtype (pandemic)	Phase I www.vaxinnate.com
VGX-3100 (HPV type 16/18 DNA vaccine)	Inovio Pharmaceuticals *Blue Bell, PA*	human papillomavirus infection (see also cancer)	Phase II www.inovio.com
VGX-3400 (DNA vaccine)	Inovio Pharmaceuticals *Blue Bell, PA*	prevention of influenza A virus H5N1 subtype	Phase I www.inovio.com
visceral leishmaniasis vaccine	Infectious Diseases Research Institute *Seattle, WA*	visceral leishmaniasis	Phase I www.idri.org

Infectious Diseases

Product Name	Sponsor	Indication	Development Phase
VRC-HIVADV014-00-VP (HIV-1 recombinant adenovirus vaccine)	GenVec *Gaithersburg, MD* Vaccine Research Center (NIAID) *Bethesda, MD*	prevention of HIV infection	Phase II completed www.genvec.com
VRC-HIVADV027-00-VP (HIV adenovector Ad35 vaccine)	GenVec *Gaithersburg, MD* Vaccine Research Center (NIAID) *Bethesda, MD*	prevention of HIV infection	Phase I www.genvec.com
VRC-HIVDNA016-00-VP (HIV adenovector Ad35 vaccine)	Vaccine Research Center (NIAID) *Bethesda, MD*	prevention of HIV infection	Phase I www.vrc.nih.gov

Neurological Disorders

Product Name	Sponsor	Indication	Development Phase
AD02 vaccine (amyloid-beta protein inhibitor)	Affiris *Vienna, Austria* GlaxoSmithKline *Rsch. Triangle Park, NC*	Alzheimer's disease	Phase II www.affiris.com www.gsk.com
AD03 vaccine (amyloid-beta protein inhibitor)	Affiris *Vienna, Austria* GlaxoSmithKline *Rsch. Triangle Park, NC*	Alzheimer's disease	Phase I www.affiris.com www.gsk.com
ATX-MS-1467 (synthetic peptide-based vaccine)	EMD Serono *Rockland, MA*	multiple sclerosis	Phase I www.emdserono.com
BHT-3009 (DNA vaccine)	Bayhill Therapeutics *Palo Alto, CA*	relapsing-remitting multiple sclerosis	Phase II completed www.bayhilltx.com
CAD106 (amyloid beta-protein inhibitor)	Novartis Pharmaceuticals *East Hanover, NJ*	Alzheimer's disease	Phase II www.novartis.com
imilecleucel-T	Opexa Therapeutics *The Woodlands, TX*	secondary progressive multiple sclerosis (Fast Track)	Phase II www.opexatherapeutics.com

Neurological Disorders

Product Name	Sponsor	Indication	Development Phase
IR208 (immunostimulant vaccine)	Immune Response BioPharma *New York, NY*	multiple sclerosis	Phase II www.immuneresponsebiopharma.com
UB-311 (liquid intramuscular amyloid beta protein inhibitor vaccine)	United Biomedical *Hauppauge, NY*	Alzheimer's disease	Phase II www.unitedbiomedical.com
V950	Merck *Whitehouse Station, NJ*	Alzheimer's disease	Phase I www.merck.com
vanutide cridificar (ACC-001/PF-05236806)	Janssen Alzheimer Immunotherapy *South San Francisco, CA* Pfizer *New York, NY*	Alzheimer's disease	Phase II www.janimm.com www.pfizer.com

Other

Product Name	Sponsor	Indication	Development Phase
AE-IG (RNA interference vaccine)	Antigen Express *Worcester, MA*	genetic disease	Phase I www.antigenexpress.com
Diamyd® autoimmune diabetes vaccine ORPHAN DRUG	Diamyd Medical *Stockholm, Sweden*	type 1 diabetes	Phase III www.diamyd.com
DiaPep277® subcutaneously-injected synthetic peptide immunomodulator ORPHAN DRUG	Andromeda Biotech *Yavne, Israel*	type 1 diabetes mellitus (newly diagnosed)	Phase III www.andromedabio.com
HLA-DQ2 peptide vaccine	ImmusanT *Cambridge, MA*	celiac disease	Phase I www.immusant.com
insulin B-chain vaccine	Orban Biotech *Brookline, MA*	type 1 diabetes mellitus	Phase I completed www.orbanbiotech.com
PF-05402536 (smoking cessation vaccine)	Pfizer *New York, NY*	smoking cessation	Phase I www.pfizer.com
PF-06413367 (smoking cessation vaccine)	Pfizer *New York, NY*	smoking cessation	Phase I www.pfizer.com
PF-06444752 (immunoglobulin-E vaccine)	Pfizer *New York, NY*	asthma	Phase I www.pfizer.com

Other

Product Name	Sponsor	Indication	Development Phase
QGE031 (anti-IgE antibody)	Novartis Pharmaceuticals *East Hanover, NJ*	bullous pemphigoid (see also allergy)	Phase II www.novartis.com
Ravax® rheumatoid arthritis vaccine	Immune Response BioPharma *New York, NY*	rheumatoid arthritis	Phase III www.immuneresponsebiopharma.com
RiVax™ ricin vaccine ORPHAN DRUG	Soligenix *Princeton, NJ*	ricin poisoning (pre-exposure)	Phase I www.soligenix.com
SEL-068 (smoking cessation vaccine)	Selecta Biosciences *Watertown, MA*	smoking cessation	Phase I www.selectabio.com
TA-CD (immunotherapeutic vaccine)	Celtic Pharma *Hamilton, Bermuda* National Institute on Drug Abuse *Bethesda, MD*	cocaine abuse	Phase II www.celticpharma.com

The content of this report has been obtained through public, government and industry sources, and the Adis "R&D Insight" database based on the latest information. **Report current as of August 16, 2013.** *The medicines in this report include medicines being developed by U.S. based companies conducting trials in the United States and abroad, PhRMA-member companies conducting trials in the United States and abroad, and foreign companies conducting clinical trials in the United States. The information in this report may not be comprehensive. For more specific information about a particular product, contact the individual company directly or go to* ***www.clinicaltrials.gov****. The entire series of Medicines in Development is available on PhRMA's website.*

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Glossary

Alzheimer's disease—Progressive and chronic deterioration of all mental functions. Early manifestations include a decrease in attention span, impaired powers of concentration, some personality change and forgetfulness. As the disease progresses, there is a loss of computational ability, in addition to word-finding problems and difficulty with ordinary activities. Ultimately, there is severe memory loss, complete disorientation, social withdrawal, loss of independence, and is fatal. It is the seventh leading cause of death in the United States.

application submitted—An application for marketing has been submitted to the U.S. Food and Drug Administration (FDA). The application can either be an NDA (new drug application) or a BLA (biologic license application).

botulism—A severe, sometimes fatal food poisoning caused by ingestion of food containing botulin and characterized by nausea, vomiting, disturbed vision, muscular weakness, and fatigue.

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 dysplasia—The abnormal growth of cells on the surface of the cervix. Although it is not cancer, it is considered a precancerous condition. Most cases of cervical dysplasia occur in women ages 25 to 35, although it can develop at any age. While all causes of cervical dysplasia are not known, most cases of cervical cancer and severe dysplasia are caused by infection of the cervix with a persistent, high-risk strain of human papillomavirus (HPV). Cervical dysplasia is also called cervical intraepithelial neoplasia, or CIN.

cervical intraepithelial neoplasia—Also called cervical dysplasia, or CIN.

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.

cytomegalovirus (CMV)—A DNA virus related to the herpes virus, affecting mostly neonatal infants and immunocompromised individuals. CMV can occur without symptoms or result in mild flu-like symptoms.

diabetes—A chronic disease due to a disturbance of the normal insulin mechanism causing problems in metabolizing sugar. Symptoms may include excessive thirst, hunger, urination and weight loss. Type 1 is the more severe form, requiring insulin treatment. Type 2, in most cases, can be controlled by a combination of dietary measures, weight loss, and oral medication.

Ebola virus—The cause of Ebola hemorrhagic (bloody) fever, a severe, often fatal disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees). Researchers believe that the virus is animal-borne (zoonotic) and is normally maintained in an animal host that is native to the African continent.

Fast Track—A process designed to facilitate the development and expedite the review of drugs to treat serious diseases and fill an unmet medical need. The status is assigned by the U.S. Food and Drug Administration. The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious diseases. Generally, determining factors include whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially superior to existing therapy. Once a drug receives Fast Track designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

glioblastoma—The most common primary brain tumor and one of the most aggressive forms of brain cancer, primarily affecting adults over the age of 50.

glioma—A type of brain tumor arising from the supporting glial cells within the brain. Gliomas make up about 60 percent of all primary brain tumors and are frequently malignant.

Haemophilus influenzae—A type of bacteria found in the respiratory tract that causes acute respiratory infections and meningitis in children but rarely in adults.

hematological malignancies—Cancers of the blood or bloodforming tissues, such as leukemia, Hodgkin's and non-Hodgkin's lymphomas, AIDS-related malignancies, multiple myeloma, myelodysplasia and myeloproliferative disorders.

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

herpes simplex virus—A strain of herpes virus that may lie dormant in nerve tissue and can be reactivated to produce painful sores of the anus or genitals.

herpes varicella zoster virus (HVZ)—Also called shingles, consists of very painful blisters on the skin and affects areas innervated by specific nerves. It may appear in adulthood as a result of having had chicken pox (caused by the varicella virus) as a child.

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.

influenza—A viral infection of the respiratory tract that causes fever, headache, muscle ache and weakness. There are three main types of influenza virus: A, B and C. A person who has had an attack with the type C virus acquires antibodies that provide immunity against that type for life. Anyone who has been infected with a certain strain of the type A or B viruses acquires immunity to that strain. Both the A- and B-type viruses occasionally alter to produce new strains that may be able to overcome immunity. Type B is fairly stable, but type A is highly unstable, and new strains of it arise constantly throughout the world.

malaria—A serious parasitic disease, spread by the bite of the Anopheles mosquito. Malaria is characterized by severe fever and chills and complications affecting the kidneys, liver, brain and blood.

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

MRSA (methicillin-resistant *Staphylococcus aureus*)—A type of bacteria that is resistant to certain antibiotics, including methicillin and other more common antibiotics such as oxacillin, penicillin and amoxicillin. Staph infections, including MRSA, occur most frequently among patients in hospitals and healthcare settings.

multiple sclerosis—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.

myeloma—A malignant condition characterized by uncontrolled proliferation of plasma cells (a class of white blood cells) in bone marrow. Symptoms include pain and destruction of bone tissue, numbness and paralysis, kidney damage, anemia, and frequent infections.

noroviruses—A group of viruses that cause the "stomach flu," or gastroenteritis. Symptoms usually include nausea, vomiting, diarrhea, and some stomach cramping. Sometimes people also have a low-grade fever, chills, headache, muscle aches, and tiredness. The illness often begins suddenly and lasts for one or two days.

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.

papillomavirus—The papillomavirus is the viral agent of warts, believed to be contagious and mostly harmless, affecting only the skin's topmost layer.

Phase 0—First-in-human trials conducted in accordance with FDA's 2006 guidance on exploratory Investigational New Drug (IND) studies designed to speed up development of promising drugs by establishing very early on whether the agent behaves in human subjects as was anticipated from preclinical studies.

Phase I—Safety testing and pharmacological profiling in humans.

Phase II—Effectiveness and safety testing in humans.

Phase III—Extensive clinical trials to demonstrate safety and efficacy in humans.

pneumococcal infections—Caused by *Streptococcus pneumoniae*, or pneumococcus, a Gram-positive human pathogenic bacterium. The organism causes many types of pneumococcal infections, including pneumonia, otitis media, meningitis, sepsis, endocarditis, and brain abscess. *S. pneumoniae* is the most common cause of bacterial meningitis in adults and children and one of the top two isolates found in ear infection (otitis media). Pneumococcal pneumonia is more common in the very young and the very old.

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.

rotavirus—A group of viruses that are wheel-like in appearance and are a major source of infant diarrhea throughout the world.

sarcoma—A malignant tumor that arises from deep body tissues, such as muscle, bone or fibrous tissue.

smallpox—A contagious, disfiguring and often deadly disease caused by the variola virus. The first symptoms of smallpox usually appear 12 to 14 days after infection. During the incubation period of seven to 17 days, an infected person looks and feels healthy and can't infect others. Following the incubation period, a sudden onset of flu-like signs and symptoms occurs, including fever, headache, severe fatigue, and sometimes vomiting, diarrhea or both. A few days later, the characteristic smallpox rash appears as flat, red spots (lesions). Within a day or two, many of these lesions turn into small blisters filled with clear fluid (vesicles) and later with pus (pustules). The rash appears first on the face, hands and forearms, and later on the trunk. The distribution of lesions is a hallmark of smallpox and a primary way of diagnosing the disease.

staphylococcal infections—Caused by *Staphylococcus* bacteria, which are germs commonly found on the skin or in the nose of healthy individuals. Most of the time, these bacteria cause no problems or result in relatively minor skin infections, but staph infections don't always remain skin-deep. In some circumstances, they may invade the bloodstream, urinary tract, lungs or heart. Skin infections caused by staph bacteria include: boils, impetigo, cellulitis, and scalded skin syndrome.

Staphylococcus aureus—A common bacterium that is a frequent cause of hospital infections, including pneumonia, surgical wounds, and systemic blood infections.

streptococcal infections—There are two types of "strep" infections—group A and group B—both of which are treated by antibiotics. Group A strep causes strep throat, scarlet fever, impetigo, toxic shock syndrome, cellulitis, and necrotizing fasciitis (flesh-eating disease). Group B 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.

tuberculosis—An infectious disease caused by the organism *Mycobacterium tuberculosis*, which is passed from person to person by breathing in airborne droplets (from coughing or sneezing). The bacteria multiply in the lungs and in some cases can spread to the lymph nodes. A person's immune system most frequently will attack and heal the infection, causing a scar on the lung.

tularemia—Also called "rabbit fever" or "deerfly fever," caused by the bacterium *Francisella tularensis* found in animals (especially rodents, rabbits, and hares). It is a potentially serious illness that can be fatal if not treated with the right antibiotics.

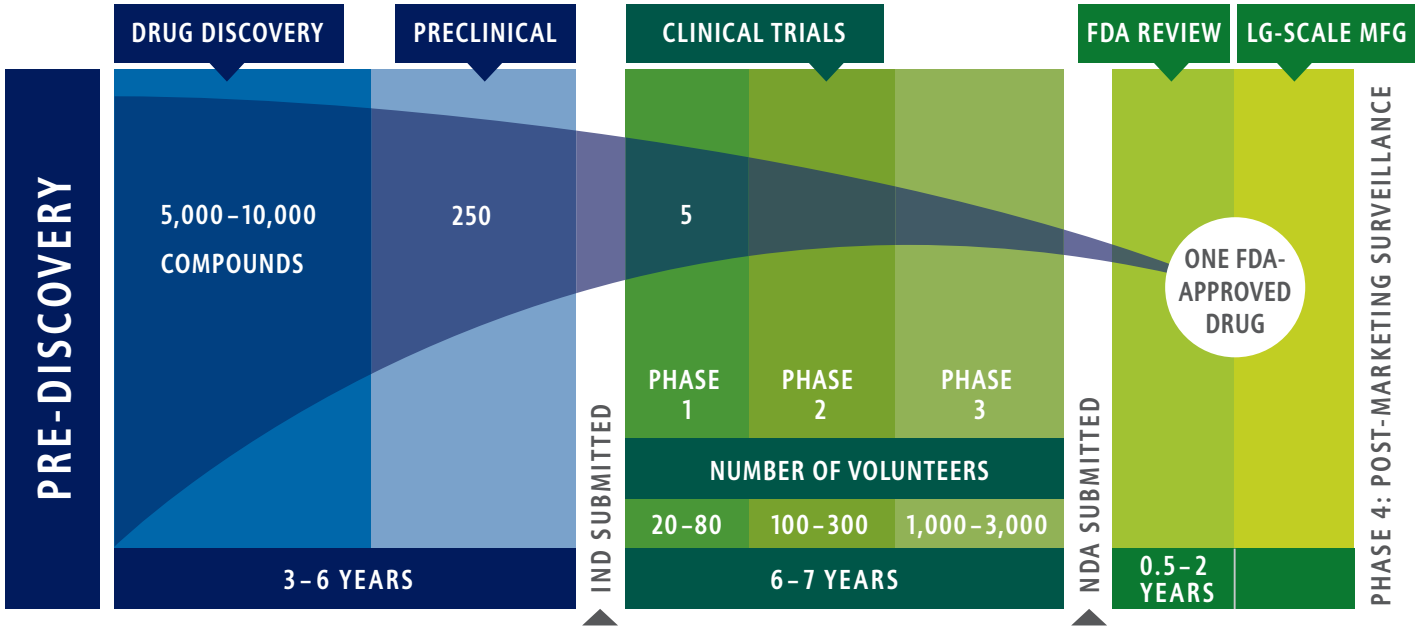
varicella zoster—Chicken pox and herpes zoster are caused by the varicella zoster virus, chicken pox being the acute invasive phase of the virus and zoster (shingles) being the reactivation of the latent stage.

Yersinia—Three Gram-negative bacilli *Yersinia* species cause infection in humans: *Y. enterocolitica* causes gastroenteritis; *Y. pseudotuberculosis* causes mesenteric lymphadenitis; and *Y. pestis* causes plague.

The Drug Discovery, Development and Approval Process

Developing a new medicine takes an average of 10-15 years;
For every 5,000-10,000 compounds in the pipeline, only 1 is approved.

Drug Discovery and Development: A LONG, RISKY ROAD



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. 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 recent 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—Researchers test the drug in a small group of people, usually between 20 and 80 healthy adult volunteers, to evaluate its initial safety and tolerability profile, determine a safe dosage range, and identify potential side effects.

Clinical Trials, Phase II—The drug is given to volunteer patients, usually between 100 and 300, to see if it is effective, identify an optimal dose, and to further evaluate its short-term safety.

Clinical Trials, Phase III—The drug is given to a larger, more diverse patient population, often involving between 1,000 and 3,000 patients (but sometime many more thousands), to generate statistically significant evidence to confirm its safety and effectiveness. They are the longest studies, and usually take place in multiple sites around the world.

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 $48.5 billion in research and development in 2012.