Medicines in Development

COPD

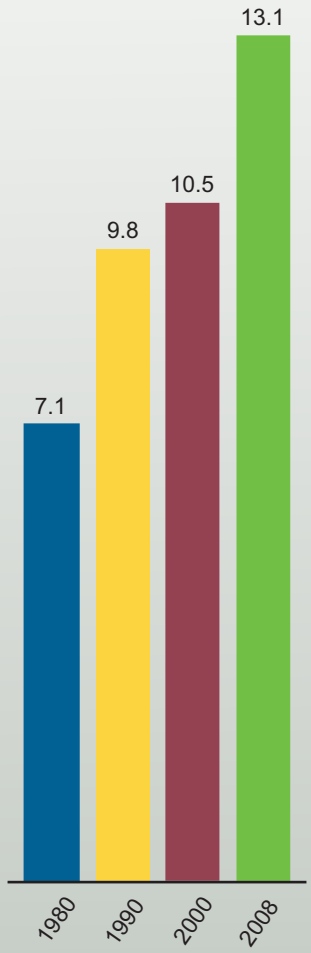
PRESENTED BY AMERICA'S BIOPHARMACEUTICAL RESEARCH COMPANIES

2012 REPORT

More Than 50 Medicines in Pipeline for Third Leading Cause of Death in the United States

COPD Prevalence in the United States

(in millions)



Source: U.S. Centers for Disease Control and Prevention

Today, more than 13 million American adults are suffering from chronic obstructive pulmonary disease (COPD), leading to limitations in their ability to work, exercise and perform normal social activity. COPD, a chronic lower respiratory disease that includes chronic bronchitis and emphysema, is characterized by obstruction of airflow to the lungs that interferes with normal breathing.

America's biopharmaceutical research companies have 54 medicines for treating COPD in the later stages of the pipeline, meaning they are either in clinical trials or awaiting FDA review.

Each year, more than 120,000 Americans die from the disease. In addition to robbing millions of patients of their ability to breathe normally, COPD costs the nation approximately $49.9 billion, including direct healthcare costs and other indirect costs, according to the National Institutes of Health.

While smoking is the main risk factor for COPD, and nearly 90 percent of COPD deaths are caused by smoking, other causes include air pollution, second-hand smoke, occupational dusts and chemicals, hereditary and childhood respiratory infections.

America's biopharmaceutical researchers are exploring various new ways to attack this devastating disease. Examples of new approaches to treating COPD include:

- An adult stem cell therapy that targets a protein in the blood that is often elevated in COPD.
- A monoclonal antibody that acts on IL-1 receptors involved in inflammatory conditions.
- A medicine that targets the underlying inflammation in COPD.

The quest for new medicines is intense and financially risky. Each new medicine costs, on average, more than $1 billion and takes 10 to 15 years to develop. But new scientific advances are increasing our knowledge, and researchers are using every cutting-edge tool at their disposal to find new treatments and potential cures.

PhRMA

Chronic Obstructive Pulmonary Disease (COPD)

Product Name	Sponsor	Indication	Development Status*
aclidinium inhalation	Almirall *Barcelona, Spain* Forest Laboratories *New York, NY*	chronic obstructive pulmonary disease (COPD)	application submitted (800) 678-1605
aclidinium/formoterol inhalation	Almirall *Barcelona, Spain* Forest Laboratories *New York, NY*	COPD	Phase III (800) 678-1605
AM211	Panmira Pharmaceuticals *San Diego, CA*	COPD	Phase I (858) 875-4810
AZD1981 (CRTh2 receptor antagonist)	AstraZeneca *Wilmington, DE*	COPD	Phase II (800) 236-9933
AZD 2115 (MABA)	AstraZeneca *Wilmington, DE*	COPD	Phase I (800) 236-9933
AZD2423 (CCR2b antagonist)	AstraZeneca *Wilmington, DE*	COPD	Phase II (800) 236-9933
AZD3199 (iLABA)	AstraZeneca *Wilmington, DE*	COPD	Phase II (800) 236-9933
AZD5069 (CXCR2)	AstraZeneca *Wilmington, DE*	COPD	Phase II (800) 236-9933
AZD5423 (inhaled SEGRA)	AstraZeneca *Wilmington, DE*	COPD	Phase II (800) 236-9933
AZD8683 (muscarinic antagonist)	AstraZeneca *Wilmington, DE*	COPD	Phase I (800) 236-9933
BCT197	Novartis Pharmaceuticals *East Hanover, NJ*	COPD	Phase II (888) 669-6682
BI-137882	Boehringer Ingelheim Pharmaceuticals *Ridgefield, CT*	COPD	Phase I (800) 243-0127
BIO-11006	BioMarck Pharmaceuticals *Durham, NC*	COPD	Phase II www.biomarck.com
Dulera® mometasone/formoterol	Merck *Whitehouse Station, NJ*	COPD	application submitted (800) 672-6372

* For more information about a specific medicine in this report, please call the telephone number listed.

Chronic Obstructive Pulmonary Disease (COPD)

Product Name	Sponsor	Indication	Development Status*
EP-101 (LAMA)	Elevation Pharmaceuticals *San Diego, CA*	COPD	Phase II (858) 436-1616
EP-102 (LAMA/LABA)	Elevation Pharmaceuticals *San Diego, CA*	COPD	Phase II (858) 436-1616
EPI-12323	EpiGenesis Pharmaceuticals *Cranbury, NJ*	COPD	Phase II (609) 409-6080
formoterol/fluticasone fixed-dose combination (inhalation)	Dey Pharma *Basking Ridge, NJ*	COPD	Phase II (908) 542-1999
GSK256066 (inhaled PDE4 inhibitor)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase II (888) 825-5249
GSK573719 (muscarinic acetylcholine antagonist)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase III (888) 825-5249
GSK573719/vilanterol (muscarinic acetylcholine antagonist/long-acting beta2 agonist)	GlaxoSmithKline *Rsch. Triangle Park, NC* Theravance *South San Francisco, CA*	COPD	Phase III (888) 825-5249 (877) 275-8479
GSK610677 (inhaled p38 kinase inhibitor)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase I (888) 825-5249
GSK961081 (muscarinic antagonist/ beta2 agonist)	GlaxoSmithKline *Rsch. Triangle Park, NC* Theravance *South San Francisco, CA*	COPD	Phase II (888) 825-5249 (877) 275-8479
GSK1325756 (chemokine receptor antagonist-2)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase I (888) 825-5249
GSK2245840 (SIRT1 activator)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase I (888) 825-5249
Ilaris® canakinumab	Novartis Pharmaceuticals *East Hanover, NJ*	COPD	Phase I/II completed (888) 669-6682
LAS 100977 (LABA)	Almirall *Barcelona, Spain* Forest Laboratories *New York, NY*	COPD	Phase II (800) 678-1605
levosalbutamol/ipratropium inhalation solution	Sunovion Pharmaceuticals *Marlborough, MA*	COPD	Phase II (508) 481-6700

Chronic Obstructive Pulmonary Disease (COPD)

Product Name	Sponsor	Indication	Development Status*
losmapimod (oral p38 kinase inhibitor)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase II (888) 825-5249
MEDI-2338 (anti-IL-18 mAb)	MedImmune *Gaithersburg, MD*	COPD	Phase I (301) 398-0000
MEDI-8968 (anti-IL-1R)	MedImmune *Gaithersburg, MD*	COPD	Phase I (301) 398-0000
MK-7123 (navarixin)	Ligand Pharmaceuticals *La Jolla, CA* Merck *Whitehouse Station, NJ*	COPD	Phase II (858) 550-7500 (800) 672-6372
MN-166 (ibudilast)	MediciNova *San Diego, CA*	COPD	Phase I completed (858) 373-1500
MN-221 (bedoradrine)	MediciNova *San Diego, CA*	COPD	Phase I (858) 373-1500
NVA237 (glycopyrrolate inhalation)	Novartis Pharmaceuticals *East Hanover, NJ*	COPD	Phase III (888) 669-6682
O-desulfated heparin intravenous	ParinGenix *Tucson, AZ*	COPD	Phase II (617) 480-5068
olodaterol	Boehringer Ingelheim Pharmaceuticals *Ridgefield, CT*	COPD	Phase III (800) 243-0127
olodaterol/tiotropium bromide	Boehringer Ingelheim Pharmaceuticals *Ridgefield, CT*	COPD	Phase II (800) 243-0127
paclitaxel-loaded stent	Broncus Technologies *Mountain View, CA*	emphysema	Phase III (650) 428-1600
PF-03715455	Pfizer *New York, NY*	COPD	Phase I (860) 732-5156
PH-797804	Pfizer *New York, NY*	COPD	Phase II (860) 732-5156
Prochymal® remestemcel-L	Osiris Therapeutics *Columbia, MD*	COPD	Phase II (443) 545-1800

Chronic Obstructive Pulmonary Disease (COPD)

Product Name	Sponsor	Indication	Development Status*
PT001 (glycopyrrolate inhalation aerosol)	Pearl Therapeutics *Redwood City, CA*	COPD	Phase II (650) 305-2600
PT003 (glycopyrrolate/formoterol inhalation aerosol)	Pearl Therapeutics *Redwood City, CA*	COPD	Phase II (650) 305-2600
PT005 (formoterol inhalation aerosol)	Pearl Therapeutics *Redwood City, CA*	COPD	Phase II (650) 305-2600
PUR118	Pulmatrix *Lexington, MA*	COPD	Phase I (781) 357-2333
QMF149 (indacaterol/mometasone)	Novartis Pharmaceuticals *East Hanover, NJ*	COPD	Phase II (888) 669-6682
QVA149 (glycopyrrolate/indacaterol inhalation)	Novartis Pharmaceuticals *East Hanover, NJ*	COPD	Phase III (888) 669-6682
Relovair™ vilanterol/fluticasone furoate	GlaxoSmithKline *Rsch. Triangle Park, NC* Theravance *South San Francisco, CA*	COPD	Phase III (888) 825-5249 (877) 275-8479
RV568	RespiVert *London, England* Janssen Research & Development *Raritan, NJ*	COPD	Phase II (800) 526-7736
TD-4208 (LAMA)	Theravance *South San Francisco, CA*	COPD	Phase II (877) 275-8479
tetomilast	Otsuka America Pharmaceutical *Rockville, MD*	COPD	Phase II (800) 562-3974
vilanterol (long-acting beta2 agonist)	GlaxoSmithKline *Rsch. Triangle Park, NC*	COPD	Phase III (888) 825-5249
Veldona® interferon-alpha	Amarillo Biosciences *Amarillo, TX*	COPD (chronic coughing)	Phase II www.amarbio.com

Glossary

application submitted—Application for marketing has been submitted to the Food and Drug Administration (FDA).

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

emphysema—An enlargement of the tiny air sacs of the lungs (alveoli) and the destruction of their walls, which causes structural and permanent reduction of airflow.

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.

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 January 12, 2012.*** *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 web site.*

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Selected Facts about Chronic Obstructive Pulmonary Disease (COPD) in the United States

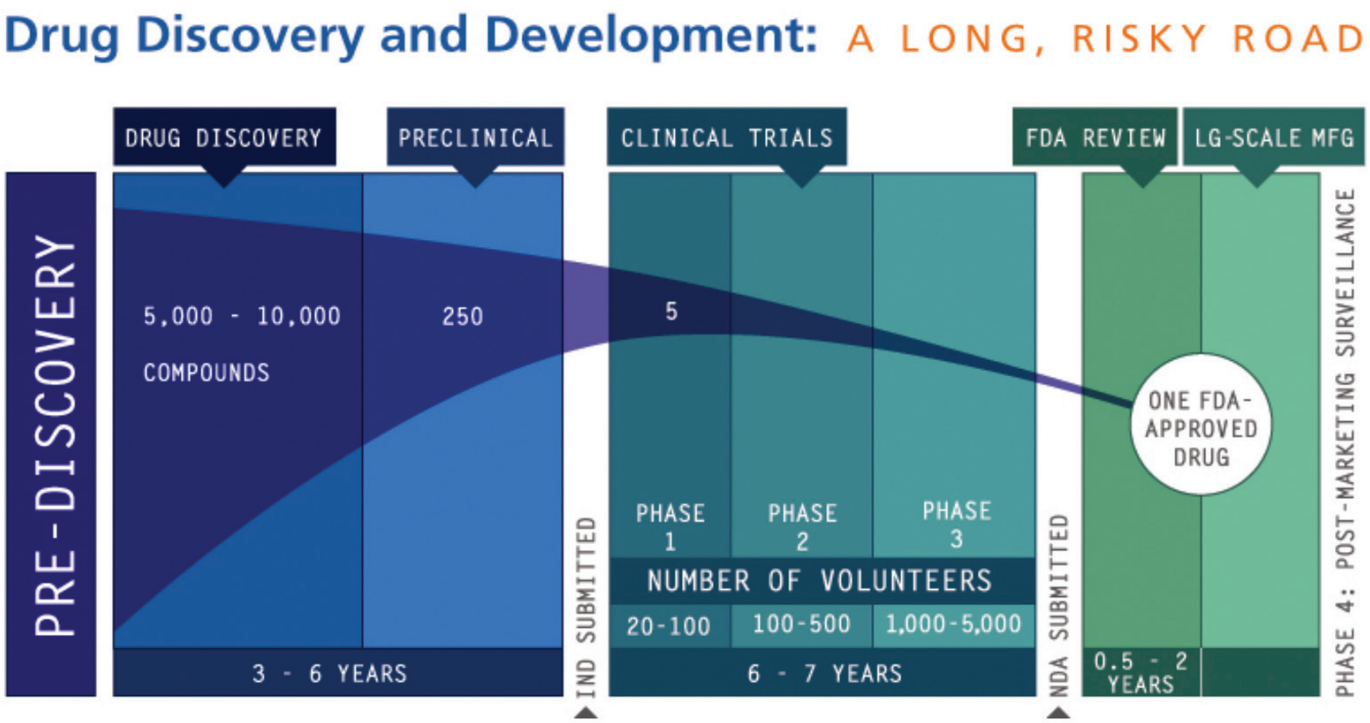
- **Chronic obstructive pulmonary disease (COPD)** is an umbrella term for progressive lung diseases, including **chronic bronchitis** and **emphysema**, that are characterized by obstruction to airflow that interferes with normal breathing. In 2008, 13.1 million U.S. adults (ages 18 and over) were estimated to have COPD. However, close to 24 million U.S. adults have evidence of impaired lung function, indicating an under diagnosis of COPD.[1]
- In 2008, an estimated 9.8 million Americans reported a physician diagnosis of **chronic bronchitis**, the inflammation and eventual scarring of the lining of the bronchial tubes. Chronic bronchitis affects people of all ages, although people age 65 and older have the highest rate at 56.3 per 1,000 population.[1]
- Females are about twice as likely to be diagnosed with **chronic bronchitis** as males. In 2008, 3.1 million males had a diagnosis of chronic bronchitis compared with 6.7 million females.[1]
- Years of exposure to the irritation of cigarette smoke usually precede the development of **emphysema**, which irreversibly damages the air sacs of the lungs and results in permanent "holes" in the tissues of the lower lungs. Of the estimated 3.7 million Americans diagnosed with emphysema, 94 percent are 45 or older.[1]
- Historically, men have been more likely than women to receive a diagnosis of **emphysema**. However, in 2008 more women (more than 2 million) reported a diagnosis of emphysema than men (almost 1.8 million).[1]
- Smoking is the primary risk factor for **COPD**. Approximately 85 percent to 90 percent of COPD deaths are caused by smoking. Female smokers are nearly 13 times as likely to die from COPD as women who have never smoked. Male smokers are nearly 12 times as likely to die from COPD as men who have never smoked.[1]
- **COPD** is the third leading cause of death in America, claiming the lives of 137,693 Americans in 2008. That was the ninth consecutive year in which women exceeded men in the number of deaths attributable to COPD. In 2008, more than 71,000 females died compared to nearly 66,000 males.[2]
- An American Lung Association survey revealed that half of all **COPD** patients (51 percent) say their condition limits their ability to work. It also limits them in normal physical exertion (70 percent), household chores (56 percent), social activities (53 percent), sleeping (50 percent), and family activities (46 percent).[1]
- In 2010, the cost to the nation for **COPD** was estimated to be approximately $49.9 billion, including $29.5 billion in direct health care expenditures, $8.0 billion in indirect morbidity costs, and $12.4 billion in indirect mortality costs.[1]

Sources:

1. American Lung Association, *www.lungusa.org*
2. U.S. Centers for Disease Control and Prevention, *www.cdc.gov*

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.



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 2007 study by the Tufts Center for the Study of Drug Development.

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

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

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

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

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

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

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

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

Discovering and developing safe and effective new medicines is a long, difficult, and expensive process. Biopharmaceutical companies invested an estimated $67.4 billion in research and development in 2010.