Biopharmaceutical Research Companies Are Developing More Than 400 Medicines for Top Chronic Diseases Affecting Older Americans

The population of Americans over 65 is on the rise, and the pace will only increase in coming years. As life expectancy continues to climb, older Americans face new and growing challenges to their health, productivity and independence from chronic conditions such as arthritis, cancer, Alzheimer’s disease, cardiovascular disease and diabetes.

Biopharmaceutical research companies are developing 465 medicines targeting the 10 leading chronic conditions affecting seniors—ischemic heart disease, diabetes, arthritis, cataracts, heart failure, depression, chronic kidney disease, osteoporosis, Alzheimer’s disease and dementia, and chronic obstructive pulmonary disease (COPD).*

The 465 medicines in development include:

- 142 for diabetes, which affects 10.9 million Americans age 65 and older;
- 92 for rheumatoid arthritis and osteoarthritis, which affects 1.3 million Americans and 12.4 million of people over age 65, respectively;
- 82 for Alzheimer’s disease, which could afflict nearly 8 million people in the United States by 2030 unless a treatment or preventative measure is found;
- 48 for heart failure (affecting 5.8 million Americans), and ischemic heart disease; and
- 40 for COPD, which impacts more than 13 million adults, with the highest prevalence rate in those over age 65.

Among the targets for other medicines in development for older Americans are cataracts, chronic kidney disease, depression and osteoporosis. All of the medicines in the report are either in human clinical trials or under review by the U.S. Food and Drug Administration. Facts about these leading chronic conditions in seniors can be found on page 5.

This overview highlights some of the exciting medicines listed in the report, recent gains in health outcomes, a separate report on the value of innovation in the treatment of rheumatoid arthritis, the importance of appropriate use of medicines, and the success of Medicare Part D in providing seniors with comprehensive, affordable access to medicines.

* Centers for Medicare and Medicaid Services (CMS), Chronic Condition Data Warehouse (CCW) Medicare 5% Sample, 2009.
Innovation

Many of the medicines in development for older Americans use expanded knowledge and cutting-edge technology to attack diseases in different ways. Some offer new ways to treat or prevent disease, leading to healthier lives for our nation’s seniors and potential savings to our health care system. Among the medicines listed in the report are:

- A medicine that aims to prevent or reverse progression of Alzheimer’s disease by using a human monoclonal antibody specifically designed to draw beta amyloid protein away from the brain through the blood system.
- A medication that combines two long-acting drugs allowing for once-daily dosing in COPD.
- A potential first-in-class medicine to treat type 2 diabetes that increases insulin secretion without causing insulin to significantly lower blood sugar.
- A medicine that recruits a patients’ own neural stem cells to repair or protect against damage to the central nervous system from stress hormones, which can lead to depression.
- A potential first-in-class medicine that targets the pain associated with osteoarthritis by inhibiting a gene-encoding protein that plays a role in inflammatory pain.

Healthy Aging—Science and Treatment Advances

The medicines in the pipeline follow a robust period of discovery and development of innovative medicines. In the last decade more than 300 new medicines have been approved by the FDA. These medicines are helping our nation’s seniors live longer, healthier lives. They are transforming many cancers into treatable conditions and reducing the impact of chronic diseases like cardiovascular disease, diabetes, osteoporosis and rheumatoid arthritis. And health outcomes continue to improve with the use of new medicines playing a large role in achieving better results.

- Life expectancy for men and women has increased a full decade since 1950 from 68.2 to 78.7 and it continues to steadily increase, according to the U.S. Centers for Disease Control and Prevention (CDC).

Recognizing the Value of Innovation in the Treatment of Rheumatoid Arthritis

Another new report supported by PhRMA and authored by Boston Healthcare Associates found that significant progress has been made in recent years in our ability to diagnose and treat rheumatoid arthritis (RA), a devastating autoimmune disease that causes extreme joint pain and deterioration in millions of Americans. Therapeutic advances have transformed the treatment paradigm over the last 20 years, from focusing on symptom management to now aiming for slowed disease progression and even disease remission.

This remarkable progress in RA treatment has been realized over time as our understanding of the underlying disease expands and is through a complex process of ongoing introductions of new therapeutic options and continual research on how to best use existing treatments (such as use in combination with other therapies, use earlier in the treatment line, or use with different disease indications). Often the full understanding of the therapeutic benefits of medicines is uncovered as research continues well after FDA approval.

This step-wise process by which our understanding evolves over time often reveals therapeutic benefits that were unknown or unanticipated at the time of initial FDA approval, including use in combination with other therapies, use earlier in the treatment line or disease state, and use in additional disease indications.

Combination Therapy

Since the first approval of biologic disease modifying anti-rheumatic drugs (DMARDs) in the late 1990s, research has revealed a synergistic effect when these medicines are used in combination with synthetic DMARDs. Studies have shown that a synthetic DMARD used in combination with a biologic DMARD showed greater efficacy than either treatment used alone.

Earlier Use of Therapeutics

There is a growing body of evidence that earlier initiation of therapy in the course of disease can be highly beneficial for RA patients. Long term data analysis revealed that 46 percent of patients who received treatment earlier in disease achieved remission compared to only 31 percent of patients treated at an advanced stage.

Use in Additional Disease Indications

As physicians and researchers gain an understanding of the underlying mechanism of inflammatory diseases, therapeutics initially developed for use in RA have shown efficacy in other disease indications.
• The death rate for Americans has fallen by 60 percent in the last 75 years, according to the CDC.

• Disability among seniors is down—a Harvard University study found that between 1984 and 2004/05, disability in the elderly went down by one-fifth. An elderly patient’s ability to survive a cardiovascular event without becoming disabled rose by 50 percent.

• Since 1980, life expectancy for cancer patients has increased about 3 years, and 83 percent of those gains are attributable to new treatments, including medicines, according to a study published in the *Journal of Clinical Oncology*. In 1990, cancer death rates began to fall for the first time and are continuing to decline, according to the National Cancer Institute (NCI). NCI attributes this decline to a combination of prevention, early detection, and treatment.

• According to the American Heart Association, death rates from cardiovascular disease fell 32.7 percent between 1999 and 2009. The CDC said the factors contributing to the decline in heart disease and stroke deaths were better control of risks factors, early detection, better treatment and care, including new drugs and expanded use of existing drugs.

• In recent years, eight new classes of diabetes medicines have been approved, giving patients and health care providers powerful new tools to treat the condition. Death rates for people with diabetes fell substantially—23 percent to 40 percent—between 1997 and 2006, according to the CDC.

• A recent study published in *The Lancet* found that clinical remission is now possible for patients with severe rheumatoid arthritis. When patients were treated with a combination of new and older medicines, they had a 50 percent chance of complete remission compared to 28 percent when taking only older medicines.

**Better Use of Medicines**

Successful treatment of disease with prescription medicines—whether through new innovations or existing therapies—requires appropriate use of the medicines as prescribed. Yet research shows that medicines commonly are not used as directed. Nonadherence to medicines is a major health care cost and quality problem, with numerous studies showing high rates of nonadherence directly related to poor clinical outcomes, high health care costs, and lost productivity. The cost of nonadherence has been estimated at $100 billion to $300 billion annually, including costs from avoidable hospitalizations, nursing home admissions, and premature deaths.

Adherence to treatment is especially important for management of chronic conditions. Chronic disease affects nearly one in two Americans and treating these patients accounts for $3 out of every $4 spent on medical care.

**Nearly 75 percent of adults are nonadherent—either by not filling a prescription or taking less than the dose prescribed.**

Taking medicines as prescribed helps to reduce the human toll of disease and reduce health care costs.

• Several studies have found that the increases in prescription cost-sharing are associated with about a 2 percent–6 percent decrease in medication spending. A study in the *Journal of the American Medical Association* found that doubling prescription copays reduce adherence by up to 45 percent.

• Seniors who are subject to annual prescription benefit caps were less likely to use medicines appropriately, and experienced unfavorable clinical outcomes, including poor control of blood pressure, cholesterol levels, and glucose levels as a result, according to a study in the *New England Journal of Medicine*.

• A study in the *Archives of Internal Medicine* found that increased cost sharing delayed the initiation of medication treatment for elderly patients who were newly diagnosed with a chronic illness—when copays were doubled in the retiree health plan, the percentage of patients newly diagnosed with hypertension who started treatment fell in one year from 54 percent to 40 percent.

• Diabetes patients who do not consistently take their medicines as prescribed are 2.5 times more likely to be hospitalized than those who follow the prescribed treatment regimen more than 80 percent of the time.

**Improving Adherence**

• *Reducing patient out-of-pocket costs*

• *Sending patients reminders*

• *Pharmacist-led interventions*

• *Education and behavioral support*

• *Synchronization of multiple prescriptions*
OVERVIEW  •  Medicines in development OldER amERIcans

A recent study in Health Affairs found that improved adherence to diabetes medicines could avert more than 1 million emergency room visits and nearly 620,000 hospitalizations annually, for a total savings of $8.3 billion.

Nonadherent patients with high blood pressure were 7 percent, 13 percent and 42 percent more likely to develop coronary artery disease, cerebrovascular disease and chronic heart failure, respectively, over a 3-year period when compared to patients who took their medicines as prescribed.

Medicare Part D—A Success for Patients and Health Care System

Just as better use of medicines is essential to the successful prevention, management and treatment of disease, good access to a wide range of medicines across therapeutic categories is paramount to improved health outcomes and system-wide savings. The Medicare prescription drug program (Part D) is answering this call with great results.

At the time the Medicare Part D was launched, some questioned how the program would work. Would any plans participate? Would people sign up? Would beneficiaries get access to the medicines they needed? Ultimately, the program’s success would be judged by whether beneficiaries enrolled in plans that met their needs and whether the program’s costs were held within reasonable limits.

Now in its eighth year, Medicare Part D is exceeding expectations. An extensive body of research attests to the program’s successes.

• Satisfaction rate among beneficiaries is 90 percent.
• Low-income seniors have access to medicines at little or no cost.
• Recent studies show Part D has lowered Medicare spending by helping patients avoid costly hospitalizations and other health care services.

Part D has been a success for seniors and taxpayers due to its market-based, competitive structure, in which prices are negotiated by large powerful private plans—the same plans used by corporate employers and insurers—on behalf of seniors and taxpayers.

Seniors’ average Part D premium have been flat at about $30 per month for the last three years—about 50 percent lower than initial projections, according to the Centers for Medicare and Medicaid Services. The bipartisan Congressional Budget Office (CBO) recently reported that Part D has cost 45 percent less than originally expected. CBO also recently indicated that Part D is the single biggest factor responsible for lower overall Medicare spending growth projections.

A study published in the Journal of the American Medical Association demonstrated that the implementation of Medicare Part D was associated with $1,200 in reduced nondrug medical spending per beneficiary per year in the first two years of the program among beneficiaries with prior limited or no drug coverage. Coupled with other research showing that nearly 11 million seniors gained comprehensive prescription drug coverage through Part D, this represents an overall savings of $13 billion in 2007, the first year of enrollment in the program.

Relatedly, CBO recently confirmed that the use of medicines helps to reduce other Medicare costs. Citing a “substantial body of evidence,” CBO announced a major change to its cost-estimating methodology that will credit policies that increase the use of prescription medicines in Medicare with savings on other medical costs in Parts A and B. America’s health care system faces many difficult economic challenges. Medicare Part D, in contrast, stands as an example of how a market-based health care program runs efficiently and delivers the services and treatments it promised.

The more than 400 medicines in the pipeline targeting myriad chronic diseases provide new hope to older Americans seeking to live longer, more independent and healthier lives. Programs such as Medicare Part D help ensure that seniors have access to the medicines they need to prevent, manage and treat disease.

Medicare Part D Saves Money

- 45% below original cost estimate
- $100 billion program cost savings
- $13 billion saved in hospital care
## Selected Facts about Chronic Diseases Among Seniors

### Alzheimer’s Disease and Other Dementias

- An estimated 5.4 million Americans have Alzheimer’s disease (AD). Today, someone in America develops AD every 68 seconds. By 2050, there is expected to be one new case of AD every 33 seconds, or nearly a million new cases per year, and AD prevalence is projected to be 11 million to 16 million.
- AD is the sixth leading cause of death in the United States and the fifth leading cause of death in Americans age 65 and older.
- Medicare payments for services to beneficiaries age 65 and older with AD and other dementias are three times as great as payments for beneficiaries without those conditions, and Medicaid payments are 19 times as great. In 2012, payments for health care, long-term care, and hospice services for people age 65 and older with AD and other dementias were estimated to be $200 billion (not including the contributions of unpaid caregivers, which were valued at more than $210 billion).

### Arthritis

- An estimated 26.9 million U.S. adults suffer from osteoarthritis (OA), and 12.4 million of them are age 65 and older.
- Job-related OA costs $3.4 billion to $13.2 billion per year.
- In the United States, rheumatoid arthritis (RA) affects 1.3 million people.
- The average age of people with prevalent RA has increased steadily over time, from 63.3 years in 1965 to 66.8 years in 1995, suggesting that RA has become a disease of older adults.
- Nearly $128 billion is spent each year in medical care and indirect expenses, including lost wages and productivity due to arthritis, including RA.

### Cataracts

- Cataracts affect nearly 22 million Americans age 40 and older. By age 80, more than half of all Americans have cataracts.
- Direct medical costs for cataract treatment are estimated to be $6.8 billion annually.

### Chronic Kidney Disease

- More than 26 million people (13 percent) in the United States have chronic kidney disease (CKD), and most are undiagnosed. Another 20 million are at increased risk for CKD.
- The prevalence of CKD is higher with older age: 5.7 percent for those ages 20 to 39, 9.1 percent for those ages 40 to 59, and 35.0 percent for those age 60 and older.

### Chronic Obstructive Pulmonary Disease (COPD)

- In 2008, 13.1 million U.S. adults (age 18 and older) were estimated to have chronic obstructive pulmonary disease (COPD). However, close to 24 million U.S. adults have evidence of impaired lung function, indicating an under diagnosis of COPD.
- COPD is the third leading cause of death in America, claiming the lives of 124,477 Americans in 2007.
- 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.
Selected Facts about Chronic Diseases Among Seniors (continued)

Depression

- **Depression** affects more than 6.5 million of the 35 million Americans age 65 and older, and it occurs 70 percent more frequently in women than in men.\(^8\)
- **Depression** is the single most significant risk factor for suicide in the elderly population. White males age 85 and older consistently have the highest suicide rate than any other age and ethnic group in the United States.\(^9\)
- **Clinical depression** has become one of America’s most costly illnesses. Left untreated, depression costs more than $51 billion in absenteeism from work and lost productivity and $26 billion in direct treatment costs. More than 80 percent of people with clinical depression can be successfully treated.\(^10\)

Diabetes\(^11\)

- In the United States, 25.8 million people, or nearly 8.3 percent of the population, have **diabetes**.
- Among those people age 65 years and older, 10.9 million, or 26.9 percent, have **diabetes**.
- **Diabetes** is the seventh leading cause of death in the United States.
- The total annual economic cost of **diabetes** in 2007 was $174 billion.

Heart Failure

- About 5.8 million people in the United States have **heart failure** and that number is growing. Heart failure is more common in people who are age 65 or older. Men have a higher rate of heart failure than women.\(^12\)
- The total direct and indirect costs of **cardiovascular disease** and stroke in the United States for 2009 was estimated to be $312.6 billion.\(^6\)

Osteoporosis\(^13\)

- About 10 million Americans have **osteoporosis**, and some 34 million are at risk for the disease. Estimates suggest that about half of all women older than age 50, and up to one in four men, will break a bone because of osteoporosis.
- **Osteoporosis** is responsible for 2 million broken bones and $19 billion in related costs every year. By 2025, experts predict that osteoporosis will be responsible for approximately 3 million fractures and $25.3 billion in costs each year.

Sources:

1. Alzheimer’s Association, [www.alz.org](http://www.alz.org)
2. U.S. Center for Disease Control and Prevention, [www.cdc.gov](http://www.cdc.gov)
3. Arthritis Foundation, [www.arthritis.org](http://www.arthritis.org)
4. American College of Rheumatology, [www.rheumatology.org](http://www.rheumatology.org)
10. Mental Health America, [www.mentalhealthamerica.net](http://www.mentalhealthamerica.net)
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 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 $49.5 billion in research and development in 2011.